Anaesthesia

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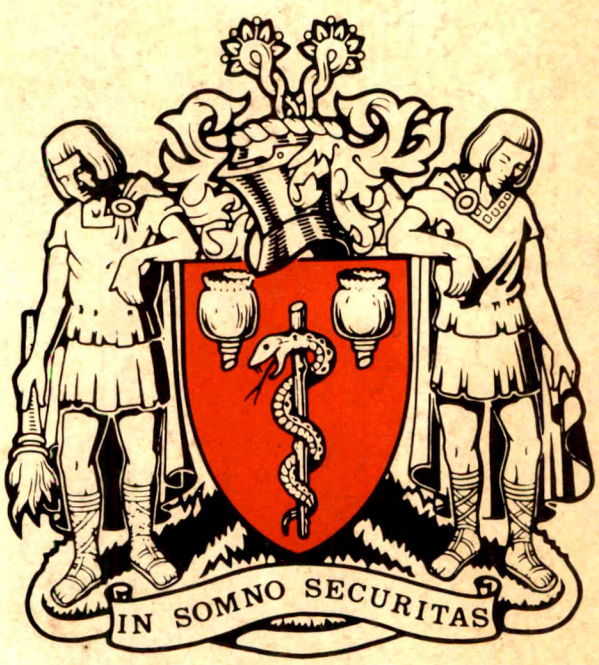

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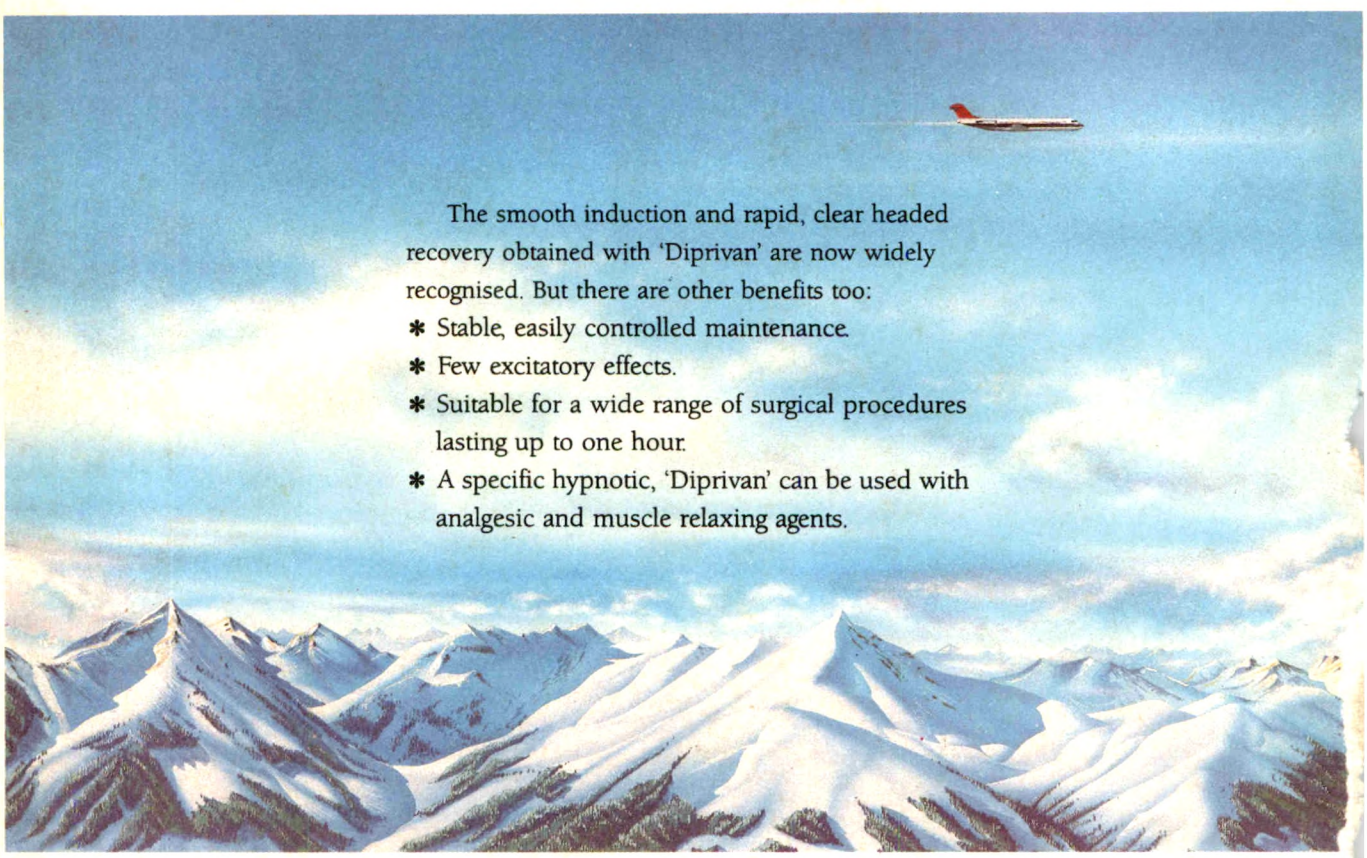

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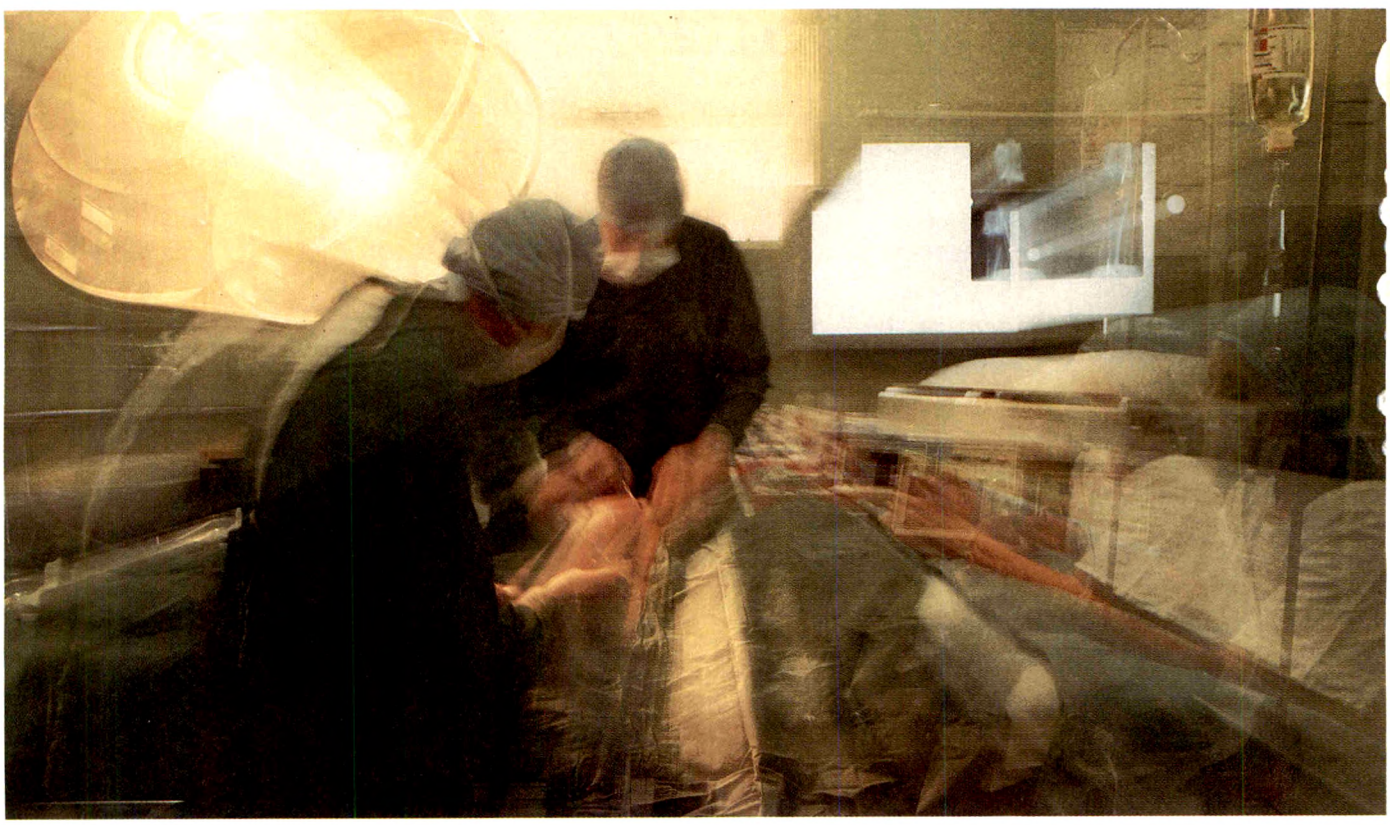

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BEHRING

Anaesthesia, 1990, Volume 45, pages 351–352

Editorial

Awareness during anaesthesia: what should the patient be told?

Patients who undergo general anaesthesia expect to remember none of the events between induction of anaesthesia and recovery of consciousness after completion of surgery. However, probably up to 0.5% of those who receive muscle relaxants as part of the anaesthetic technique are able to recall intra-operative events spontaneously. The incidence can be reduced by the avoidance of errors but it is unlikely that awareness of this type can be eliminated totally without unduly endangering some patients by administration of excessive amounts of anaesthetic agents.[1] The majority of patients who recall intra-operative events do not remember pain, and many do not realise that the events which they recollect occurred during operation. However, about 10% of patients who are able to recall events have experienced pain,[2] and others may be distressed also, particularly if they remember a feeling of paralysis. Most patients who are distressed report their experience during the first few postoperative days; commonly, a relative is told in the first instance and the ward nurses may be informed. If the anaesthetist is notified, there is a natural tendency either to ignore the complaint, or to deny that awareness has occurred and to suggest that the patient was dreaming. This approach is unwise for two reasons.

The first reason relates to the psychological sequelae of awareness. A patient who has been aware and experienced pain has undergone an extremely traumatic experience. It is recognised that a form of neurosis, which includes insomnia, anxiety, irritability, repetitive nightmares, depression and a preoccupation with death, may result and there may be a morbid fear of hospitals, doctors and, in particular, of the need for future operations.[3-5] The psychological condition of the patient may be made worse if relatives or hospital staff suggest that the experience was imagined. Indeed, in most cases the neurosis is ameliorated or cured if the patient is assured that the memories are genuine.

The second reason is associated with medicolegal consequences for the anaesthetist. In 1985 and in 1989, two women who were aware of pain during Caesarean section were awarded sums of £13 000 and £18 000, and each case was surrounded by intense publicity. Currently, the medical defence organisations are dealing with a large number of similar claims. A recent television programme[6] again brought the subject into the public eye. One of the principal complaints of the patients interviewed on that programme (all of whom were pursuing a claim for medical negligence) was that they had never received an explanation of the cause of the alleged episode of awareness, and it was suggested that legal proceedings might have been avoided if the anaesthetists concerned had listened sympathetically and explained why awareness had occurred.

It must be recognised that not all such protestations from plaintiffs are genuine; some plaintiffs are determined to pursue a claim with the prospect of financial reward despite having received a full explanation and apology. Nevertheless, others are motivated primarily by the feeling that their trust in the anaesthetist has been betrayed. Whether the complaint is genuine or fictitious, animosity and bitterness at the apparent lack of concern by staff tend to magnify and exaggerate the patient's memories with the passage of time, and as many of the complaints are of a subjective nature they may be difficult to refute if a legal claim proceeds. Judgment was made against the plaintiff in a recent High Court action in which negligence against an anaesthetist was claimed on the basis of alleged awareness during Caesarean section;[7] however, the judge criticised the Health Authority for failing to ensure that the anaesthetist was informed of the patient's complaint and suggested that the claim, which had been traumatic for both the anaesthetist and the patient, would not in all probability have been pursued if satisfactory communications had been established in the early postoperative period.

Clearly, the risks of psychological sequelae for the patient and the trauma of medicolegal proceedings against the anaesthetist will be minimised if awareness is avoided. Awareness is preventable in the majority of cases. Many cases arise from malfunction of equipment, but nearly all of these could be avoided by meticulous inspection of apparatus before anaesthesia and (or) vigilance during operation. A substantial proportion of cases are the result of administration of inappropriately low concentrations of anaesthetic agents; these could be averted by education of anaesthetists. However, in some cases, awareness does occur when an appropriate technique is employed and when no clinical signs of inadequate anaesthesia are present. It should be noted that it is virtually impossible to defend any claim of negligence arising from alleged awareness unless there is a comprehensive anaesthetic record which details the doses, concentrations and timings of *all* drugs as well as frequent recordings of clinical observations and measurements.[8]

What should be done if a patient complains of awareness? There is clearly a need to educate both nurses and medical staff in other disciplines so that the anaesthetist is informed invariably if a complaint occurs; however, problems arising from poor communications would be obviated if anaesthetists visited and talked to all their patients in the postoperative period. In any event, the anaesthetist must *always* visit the patient if (s)he is told that a complaint of awareness is made. (S)he should listen to the patient's complaint and try by indirect and direct questioning to ascertain whether the memories are genuine. It is clear in some cases that the patient has experienced an unpleasant dream. Dreams rarely involve details of an operation; more commonly, some other traumatic event is remembered, although there may be associations of some sort with surgery. There may be a relationship between dreams and light anaesthesia,[9] although dreaming may take place at any time in the peri-operative period. If pain associated with the operative wound has been experienced, the anaesthetist should try to elicit whether the experience has occurred during or after surgery; pain in the immediate postoperative period, together with confusion resulting from residual anaesthetic and analgesic agents, may result in

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the experience being attributed to an intra-operative event. Rarely, events which are compatible with recall during operation may be recounted in a totally fictitious complaint. However, the large majority of patients who claim to recall intra-operative events are genuine, and remember specific occurrences which are unique to their procedure, e.g. corroborated items of conversation, the position of their limbs, etc. Many of these patients do not remember pain, but may be distressed nevertheless. Those who recall pain are often distraught. The anaesthetist should firstly acknowledge the fact that (s)he believes the patient's account of events. (S)he should explain that awareness can occur without fault during anaesthesia in which muscle relaxants are employed because of the desire to avoid high and potentially toxic doses of anaesthetic agents and because of difficulty in interpreting clinical signs. (S)he should apologise to the patient and offer an assurance that the occurrence of awareness will be recorded in the hospital notes so that other anaesthetists will know of the problem if surgery is required in the future. If it is clear that an avoidable error has caused awareness, it may be argued that it should not be acknowledged lest this is taken to imply admission of negligence. However, it is my view that such an error should be admitted if awareness has occurred, as this may serve to reduce the patient's fears about awareness during subsequent operations. The interview should in all instances be conducted in the presence of a witness, and an explicit summary of the conversation should be recorded in the hospital notes. Junior anaesthetists should, whenever possible, interview the patient in the presence of a consultant anaesthetist. It might be beneficial if a consultant with a special interest in awareness was asked to counsel the patient.

Should patients be warned of the possibility of awareness before general anaesthesia? It has been suggested. that to do so would upset patients to a degree which must be to their disadvantage.[1,10] However, because of recent publicity, many patients are now familiar with the fact that awareness can occur, assume that it is always associated with excruciating pain and may already have considerable anxiety on this account when they present for surgery. Many obstetric patients now ask directly about awareness. Consequently, I believe that there is now a strong argument in favour of discussing awareness at the pre-operative visit, possibly with every patient but particularly with the high-risk patient, or before Caesarean section. Certainly, any patient who asks directly before operation about awareness must be given an honest and frank explanation.

Finally, it may be felt by some that the sequelae of awareness during general anaesthesia justify an increase in the use of regional techniques. However, the failure rate associated with regional blocks is considerably higher than that with general anaesthesia.[11] An increasing number of patients in the United Kingdom find discomfort or pain of any magnitude unacceptable during surgery carried out under regional anaesthesia, and some now complain that an unsuccessful regional block, or the subsequent need for 'unnecessary' general anaesthesia, is the result of negligence on the part of the anaesthetist. There may be arguments against warning patients about awareness before general anaesthesia, but *all* patients in whom regional anaesthesia is planned should be warned of the possibility of partial or total failure, and that both pain and discomfort may be experienced during surgery.

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Editorial notices

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Anaesthesia, 1990, Volume 45, pages 353–356

Recovery of bowel motility after high dose fentanyl or morphine anaesthesia for cardiac surgery

H. YUKIOKA, M. TANAKA AND M. FUJIMORI

Summary

Recovery of bowel function was investigated after cardiac surgery. The time to first passage of flatus was measured using a carbon dioxide analyser as an indication of the return of coordinated bowel motility in 22 adult patients who received high-dose fentanyl (56.3, SD 20.9 μg/kg) or morphine (1.3, SD 0.7 mg/kg) anaesthesia. The time from the patient's arrival in the intensive care unit to passage of the first flatus in patients who received fentanyl anaesthesia was significantly longer than in those who received morphine ($p < 0.05$). There was a significant relationship between the time to first flatus and the total dose of fentanyl, but no such relationship could be demonstrated for morphine. It is concluded that high-dose fentanyl anaesthesia delays recovery of bowel motility in a dose-dependent manner.

Key words

Analgesics; fentanyl, morphine.
Gastrointestinal tract; flatus.

It is well known that opioid drugs depress gastrointestinal motility. However, there is little information on the recovery of bowel function after high-dose fentanyl or morphine anaesthesia for cardiac surgery. The passage of flatus has been used as an indication of the return of coordinated bowel motility after surgery.[1] In this study, we compared the effects of morphine and fentanyl on passage of flatus. Flatus contains carbon dioxide (values contained in discussion).[2] Consequently, the time to first flatus (TFF) was measured by a CO_2 analyser as described previously.[3]

Methods

The study was approved by the hospital ethics committee, and each patient gave written informed consent. Twenty-four adult patients scheduled for elective cardiac surgery were studied. The presenting diagnoses were: coronary artery disease (16 patients); congenital heart disease (five patients); acquired valvular heart disease (two patients); and thoracic aortic aneurysm (one patient). Patients were allocated randomly to one of two groups to receive fentanyl or morphine anaesthesia. All patients had good left ventricular function and no gastrointestinal tract anomalies or dysfunction. Pre-operative investigations showed no severe hepatic or renal dysfunction in any patient. No patient received analgesic drugs for at least 3 days before anaesthesia. Patients fasted from midnight. Premedication consisted of either diazepam (5–15 mg) or secobarbitone (75–150 mg), and morphine (0.12 mg/kg) given intramuscularly 90 minutes before anaesthesia, followed by scopolamine (0.5 mg) or atropine (0.5 mg) given intramuscularly 30 minutes later.

Anaesthesia was induced by intravenous injection of fentanyl (14 patients) or morphine (eight patients) and the lungs were ventilated with oxygen 100%. The trachea was intubated after intravenous administration of pancuronium or vecuronium 0.12 mg/kg, plus intravenous lignocaine 1 mg/kg. Additional opioid drugs were administered intravenously immediately before sternotomy, immediately before the start of extracorporeal circulation (ECC) and, if necessary, after ECC. Muscle relaxants, nitrous oxide (50–60%) and enflurane (0.5–1%) were given when needed.

In one patient in the fentanyl group and in one patient in the morphine group, anaesthesia was induced and maintained with nitrous oxide (50–60%) and enflurane (0.5–4%) in oxygen, and pancuronium. Opioid drugs were administered immediately before sternotomy and immediately before the start of ECC.

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Table 1. Sex distribution and mean (SD) age and weight of patients.

	Age (years)	Weight (kg)	Sex (M:F)
Fentanyl	56 (11)	60 (9)	10:3
Morphine	51 (14)	63 (9)	8:1

All patients were operated on under mild or moderate haemodilution and systemic hypothermia. Dopamine (3–10 μg/kg/minute) or noradrenaline (0–0.1 μg/kg/minute) was infused after ECC. No anticholinesterase drugs were administered to reverse the effects of muscle relaxant drugs.

Mechanical ventilation was initiated after arrival in the postoperative intensive care unit (ICU) with a Servo 900C ventilator (Siemens-Elema), and a CO_2 analyser (Datex Normocap) was attached to the patient by a 200-cm narrow-bore plastic tube, taped no more than 2 cm from the anus. A deflection of more than 0.5% CO_2 was considered to indicate the passage of flatus.[3] The CO_2 analyser was linked to a Microservo SR 6411 chart recorder (Graphtec Corp.). Time from the first administration of the opioid drug (fentanyl or morphine) to passage of the first flatus (TFF-A), and time from the patient's arrival in the ICU to passage of the first flatus (TFF-B) were recorded. Total dose of fentanyl or morphine, durations of anaesthesia and ECC, and postoperative time to adequate spontaneous ventilation (tidal volume > 7 ml/kg, vital capacity > 10 ml/kg, mean inspiratory pressure < −2.0 kPa) and tracheal extubation were recorded. Postoperative time to response to verbal commands, such as 'open your eyes' was recorded.

Statistical analysis was performed using Student's *t*-test and the Chi-square test. Results were considered significant when $p < 0.05$.

Results

Two patients in the fentanyl group were discharged from ICU before passing flatus. They were excluded from analysis because they had received higher doses of fentanyl (> 70 μg/kg) despite a shorter stay (less than 10 hours) in the ICU. There were no significant differences between the two groups with respect to age, weight or sex in the remaining 22 patients in whom passage of flatus was recorded in the ICU (Table 1).

Initial intravenous mean (SD) doses of fentanyl and morphine were 32.1 (12.8) μg/kg and 0.7 (0.4) mg/kg respectively in 20 of 22 patients. Additional morphine and fentanyl were administered intravenously immediately before the sternotomy (fentanyl 9.7 (1.7) μg/kg, morphine 0.3 (0.2) mg/kg), immediately before the start of ECC (fentanyl 11.3 (3.6) μg/kg, morphine 0.4 (0.3) mg/kg) and after ECC (fentanyl 6.7 (5.7) μg/kg, morphine 0.1 (0.1) mg/kg). The time from initial to last administration of opioid drugs was 4.2 (2.4) hours in the fentanyl group and 3.9 (1.8) hours in the morphine group. The total doses of each opioid drug were fentanyl 56.3 (20.9) μg/kg, and morphine 1.3 (0.7) mg/kg respectively (Table 2).

TFF-A and TFF-B, durations of anaesthesia and ECC, and postoperative times to adequate spontaneous ventilation, to tracheal extubation and to response to verbal commands are shown in Table 2. TFF-B in the fentanyl group was significantly longer than that in the morphine group ($p < 0.05$), although there was no significant difference between the two groups in respect of TFF-A. There were no significant differences between the two groups in duration of ECC, or in postoperative times to adequate spontaneous ventilation, to tracheal extubation or to response to verbal commands. Duration of anaesthesia in the fentanyl group was significantly shorter than that in the morphine group.

There was a good correlation between TFF (A and B) and total dose of fentanyl (TFF-A: $r = 0.754$; $p < 0.005$, TFF-B: $r = 0.709$; $p < 0.01$) (Figs 1 and 2).

There was no significant correlation between TFF (A or B) and total dose of morphine (TFF-A: $r = 0.480$; NS, TFF-B: $r = 0.509$; NS) (Figs 3 and 4). There was a significant correlation between TFF-B and the duration of ECC in the fentanyl group ($r = 0.670$; $p < 0.05$), but not in the morphine group. There were no significant correlations between TFF-B and the duration of anaesthesia, or postoperative times to adequate spontaneous ventilation, to tracheal extubation, or to response to verbal commands, in either group. The duration of ECC was significantly correlated with total dose of fentanyl ($r = 0.636$; $p < 0.05$).

Table 2. Mean (SD) total dose of opioids, TFF–A*, TFF–B†, durations of anaesthesia and ECC‡, and postoperative times to response to commands, to adequate spontaneous ventilation, and to tracheal extubation.

	Fentanyl group	Morphine group	Significance
Total dose	56.3 (20.9)§	1.3 (0.7)‖	
TFF–A, hours	21.7 (8.4)	16.9 (6.6)	NS¶
TFF–B, hours	15.2 (7.3)	8.2 (6.0)	$p < 0.05$
Duration of anaesthesia, hours	6.6 (1.6)	8.8 (2.6)	$p < 0.05$
Duration of ECC, hours	1.5 (0.8)	2.0 (0.9)	NS
Postoperative time to:			
response to commands, hours	2.4 (2.2)	3.7 (3.1)	NS
adequate spontaneous ventilation, hours	9.6 (7.5)	13.5 (6.9)	NS
tracheal extubation, hours	11.3 (11.7)	13.8 (6.4)	NS

* TFF–A, time from the first administration of the opioid drug (fentanyl or morphine) to passage of the first flatus.
† TFF–B, time from the patient's arrival in the ICU to passage of the first flatus.
‡ ECC, extracorporeal circulation.
§ μg/kg.
‖ mg/kg.
¶ NS, Not significant.

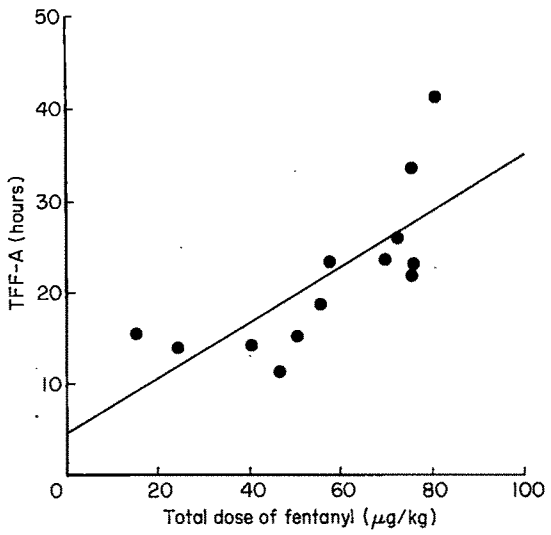

Fig. 1. Relationship between total dose of fentanyl and time from the first administration of fentanyl to passage of the first flatus (TFF-A). $y = 0.31x + 4.45$; $n = 13$; $r = 0.754$; $p < 0.005$.

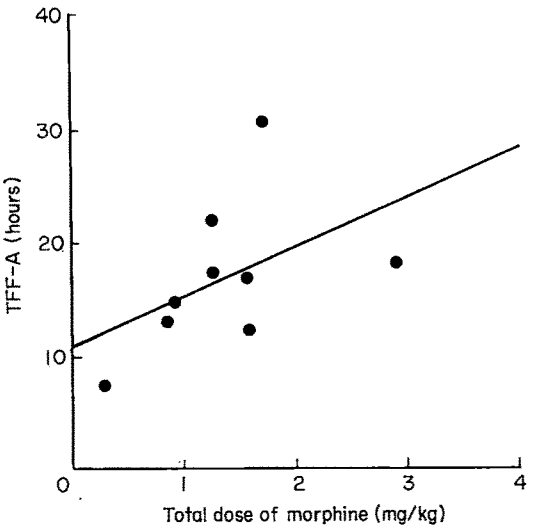

Fig. 3. Relationship between total dose of morphine and time from the first administration of morphine to passage of the first flatus (TFF-A). $y = 4.44x + 10.83$; $n = 9$; $r = 0.480$; not significant.

Discussion

High-dose fentanyl or morphine anaesthesia is used commonly for cardiac or major cardiovascular surgery because of its cardiovascular stability. We believed that it was of clinical importance to assess recovery of bowel function after high-dose opioid anaesthesia, since opioid drugs delay gastric emptying, small bowel transit and colonic transit.[4,5] The passage of flatus has been regarded as a good clinical indication of the return of coordinated bowel motility after surgery.[1] In the present study, we used a CO_2 monitor as an objective measurement of the passage of flatus. The CO_2 content of human flatus is between 5 and 80%,[3] and it has been shown that passage of flatus is measured sensitively and accurately by a CO_2 analyser in patients who would be unable to report the passage of flatus, e.g. sedated patients.

Morphine depresses coordinated bowel function in both the small intestine and colon in man. This effect seems to be dose-dependent and is seen at intramuscular morphine doses greater than 8 mg.[6] However, morphine had no effect on colonic motor activity in subhuman primates at doses of either 0.2 mg/kg or 1 mg/kg intravenously.[7] Furthermore, it is uncertain whether higher doses of intravenous morphine depress bowel motility in a dose-dependent manner. In the present study, there was no significant correlation between TFF and morphine dose, although patients with higher doses of morphine tended to have a longer TFF.

Intravenous fentanyl (2–10 nmol/kg) induced dose-related stimulation of the distal colon and associated inhibition of the proximal colon in dogs.[8] In the present study, fentanyl has been shown to depress bowel motility in a dose-dependent manner. Fentanyl is a highly lipophilic substance, and is distributed rapidly to highly perfused tissues such as muscle, lung and brain after intravenous injection.[9] The high affinity of tissues for fentanyl limits the rate of its ultimate elimination from the body by biotransformation and leads to accumulation of the drug when

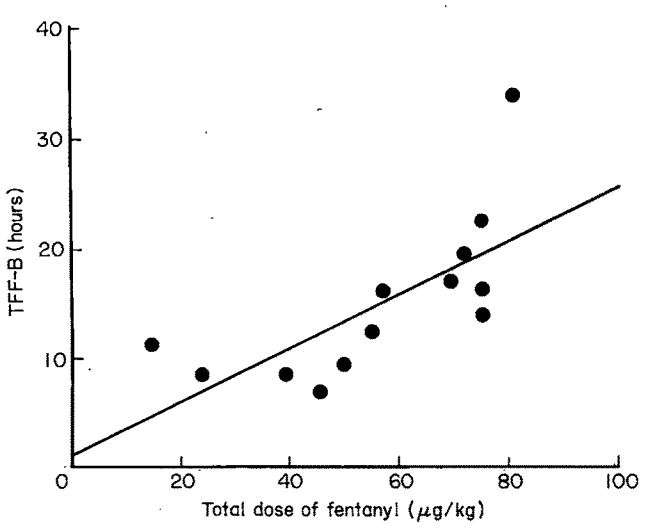

Fig. 2. Relationship between total dose of fentanyl and time from the patient's arrival in the ICU to passage of the first flatus (TFF-B). $y = 0.25x + 1.12$; $n = 13$; $r = 0.709$; $p < 0.01$.

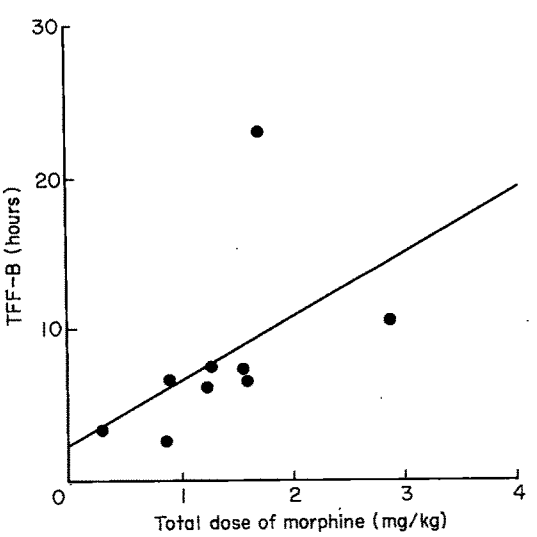

Fig. 4. Relationship between total dose of morphine and time from the patient's arrival in the ICU to passage of the first flatus (TFF-B). $y = 4.31x + 2.34$; $n = 9$; $r = 0.509$; not significant.

administered in very large or repeated doses.[10] Recovery from large doses of fentanyl takes much longer than that from small doses.[11,12] Both the intensity and duration of the effects of fentanyl are proportional to the dose.[13] Dose-dependent depression of bowel function after high-dose fentanyl anaesthesia may be associated with concentrations of fentanyl in specific central or peripheral opioid receptor sites related to intestinal motility.

In the present study, the mean TFF-B of the patients with fentanyl anaesthesia was about twice as long as that noted after morphine anaesthesia. It was reported that the decline of morphine concentrations in plasma and the appearance and excretion of conjugated morphine are similar in patients who have cardiac surgery, including ECC, to the findings in volunteers and healthy patients.[13] However, the elimination of fentanyl is prolonged in patients who undergo cardiac surgery.[14] Differences between the two drugs in TFF-B might be attributed to differences in pharmacokinetics of the drugs during cardiac surgery. Alternatively, the difference may be related to two problems encountered in this study. Firstly, the mean duration of anaesthesia in the morphine group was significantly longer than that in the fentanyl group, and this may have resulted in a lower concentration of opioid postoperatively in the morphine group; however, there was no significant difference between the two groups in respect of TFF-A. Secondly, the total dose of morphine administered was considerably less than the equianalgesic dose of fentanyl; fentanyl is believed to be 60 to 80 times more potent than morphine in man.[9] A study in which equianalgesic doses of morphine and fentanyl are used should be undertaken to compare effects of the two drugs on bowel function in detail.

In animal studies, enflurane and halothane caused cessation of colonic contractions, but recovery of normal contractile function occurred promptly after cessation of anaesthesia. Nitrous oxide is not associated with significant suppression of contractile function of the colon.[15] Patients who underwent minor surgery during anaesthesia with either halothane or enflurane and nitrous oxide in oxygen passed flatus about 2 hours postoperatively.[3] In general, the effects of volatile agents on bowel contractility diminish as anaesthesia lightens, and motility returns to normal by the time the patient regains consciousness.[4] Thus, the effects of enflurane and nitrous oxide seem unlikely to have influenced TFF in the present study.

In a previous study, premedication with diazepam and morphine delayed coordinated intestinal motility, and there was a marked delay particularly with morphine.[1] In the present study, combined effects of high-dose opioid and opioid premedication may have occurred.

There may be other factors which influenced the results of our study. Alpha- and beta-adrenergic stimulants may depress gastrointestinal motility. Alpha-receptors are predominant in the stomach and small bowel, while beta-receptors are responsible for adrenergic inhibition in the colon.[4] Increased sympathetic activity after surgery, as well as catecholamine administration, may inhibit gastrointestinal contractility during the postoperative course of cardiac surgery. The duration of ECC was significantly correlated with TFF-B in the fentanyl group in this study. Hypothermia during ECC might delay recovery of postoperative bowel motility.

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Postmortem findings after epidural anaesthesia

H. WULF AND E. STRIEPLING

Summary

Postmortem specimens of 10 patients who had received continuous epidural anaesthesia postoperatively (ranging from 2–21 days) were examined. Slight epidural haemorrhage was observed in six patients and a macroscopically visible haematoma in a thrombocytopenic patient. Nonspecific epidural inflammatory reactions were observed microscopically in all patients. Specimens from seven patients with systemic infection showed signs of epidural infection. No similar pathology was found in a control group without epidural catheters. The aetiology and risk factors of the above findings are discussed, and recommendations given to prevent such sequelae after epidural anaesthesia.

Key words

Anaesthetic techniques, regional; epidural.
Complications.

There are many reports of the advantages of continuous postoperative epidural anaesthesia and its complications.[1–4] However, only a few studies have been performed with regard to pathological anatomical sequelae.[5,6] We therefore compared the postmortem findings of a group of patients who had received continuous epidural analgesia postoperatively with those of a control group.

Methods

Four hundred and ninety-seven patients received epidural analgesia with bupivacaine 0.25–0.5% for postoperative pain relief, that lasted at least 24 hours, during the period of investigation. The epidural catheter (Portex, multiorifice type) was inserted under sterile conditions into the thoracic or lumbar area, advanced 2–3 cm, subcutaneously tunnelled, and fixed to a bacterial filter. Twenty-four patients died of causes unrelated to the epidural during this time. Informed consent was given by the relatives for a postmortem examination in 10 of these patients; this included the vertebral canal (Table 1). None of the patients had a history of spinal surgery. Insertion of the epidural catheter was without incident in all cases. Nine of these 10 patients developed septic complications in the period after catheter insertion (Table 1) and all except one (patient 2) received low-dose heparin prophylaxis.

The spinal column was removed *en bloc* for three segments above and two segments below the epidural puncture site during the autopsy. The specimens were ventrally opened in the frontal plane after treatment with 10% formalin. Subsequently, the spinal cord with its covering dura and adherent epidural tissue was dissected. Horizontal cuts of the spinal cord and its covering dura and epidural tissue were made on several levels above and below the puncture site; separate cuts of the bony vertebral canal were also made. Histological slides were prepared and subsequently stained with haematoxylin/eosin (HE) after the specimens were decalcified and embedded in paraffin. Staining with ASDCL (Naphtol-AS-D-Chloracetate-esterase) was also performed to identify granulocytes and prephase cells of the myeloblastic series.

A control group of patients without epidural catheters was also examined. These patients had suffered and died from similar diseases and also had systemic infections (Table 2).

Results

Epidural group

Table 3 presents a summary of the most important pathological findings in the vertebral canal of patients who had received epidurals. There was a moderately marked infiltration of the dura and epidural tissues with lymphocytes and plasma cells in most cases. In addition, granulocytes, taken as a sign of a distinct bacterial infection (Fig. 1), bacterial

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Table 1. Patients in epidural group (with epidural catheter).

Patient number	Age (years)	Sex	Diagnosis	Infection	Duration of epidural (days)	Interval—end of epidural till death (days)
01	45	F	Ovarian carcinoma	None	2	0
02	20	M	Acute myeloid leukaemia, bone marrow transplantation, thoracotomy	Mycotic infection	21	3
03	78	M	Perforated colonic tumour	Chronic peritonitis	9	21
04	56	M	Ruptured spleen, ileus, caecal perforation	Chronic peritonitis	14	0
05	85	M	Pleural carcinoma	Bronchopneumonia	7	0
06	75	F	Metastatic uterine carcinoma, enterostomy	Purulent peritonitis	2	47
07	71	M	Metastatic bronchial carcinoma, bowel resection	Fibrinous peritonitis	3	0
08	63	F	Pancreatic carcinoma	Purulent peritonitis	11	3
09	67	M	Cholecystectomy	Bronchopneumonia	12	0
10	38	F	Squamous cell carcinoma of the thigh	Purulent peritonitis	16	0

Table 2. Control group.

Patient number	Age (years)	Sex	Diagnosis	Infectious disease
01	75	F	Metastatic uterine carcinoma	None
02	66	M	Gall bladder perforation	Sepsis, endocarditis, purulent meningoencephalitis
03	77	M	Sigmoidectomy (carcinoma)	Chronic peritonitis
04	50	F	Chronic lymphatic leukaemia, pancreatitis	Fibrinous peritonitis
05	89	M	Pulmonary emphysema, chronic bronchitis	Bronchopneumonia
06	82	M	Perforated sigmoid carcinoma	Purulent peritonitis
07	79	F	Gastrectomy, pulmonary embolism	Fibrinous pleuritis, pericarditis
08	55	F	Metastatic pancreatic carcinoma, cholangitis	Purulent laryngotracheitis
09	75	M	Myocardial infarction	Bronchopneumonia
10	73	F	Small intestine perforation	Purulent peritonitis

growth and zones with necrosis of the dura at puncture-site level were present. A thickening along the indentations of the dura was found in some slides where the catheter had rested. Hints of a fresh extravascular accumulation of erythrocytes or older haemorrhage (haemosiderin deposition) were found in seven cases. The haematoma was macroscopically visible and spread over two to three segments in one case (patient 2). Absence of haemosiderin revealed it to be a fresh haematoma (Fig. 2).

None of the patients showed any further morphological or clinical signs of spinal compression. No pathological alterations were observed in the bones, the spinal cord and pia mater, or in the nerve roots.

Control group

Hyperaemia of the epidural space was also a common finding in the control group. Moderately marked oedema of the dura was found in one case (Table 2, patient 5). Purulent meningitis with granulocytic infiltration in the arachnoid was evident in a patient with severe septicaemia

Table 3. Histological findings in the vertebral canal of patients in the epidural group.

Microscopical findings	Patient number (see Table 1)									
	1	2	3	4	5	6	7	8	9	10
Epidural										
Hyperaemia	++	+	+	+	+	++	+	+	+	+
Fibrin		+	++		(+)			++	+	
Lymphocytes	++	++	+	+	+	(+)	+	+	+	+
Macrophages	+	+		+				(+)	+	
Giant cells		+						+	(+)	
Granulocytes	(+)			(+)	(+)		+	(+)	+	+
Bacteria		++							+	+
Haemosiderin			+	+		+				
Erythrocytes	(+)	++			+		+			
Dural										
Oedema									+	+
Necrosis		+							+	

(+), minor; +, medium; ++, distinct findings.

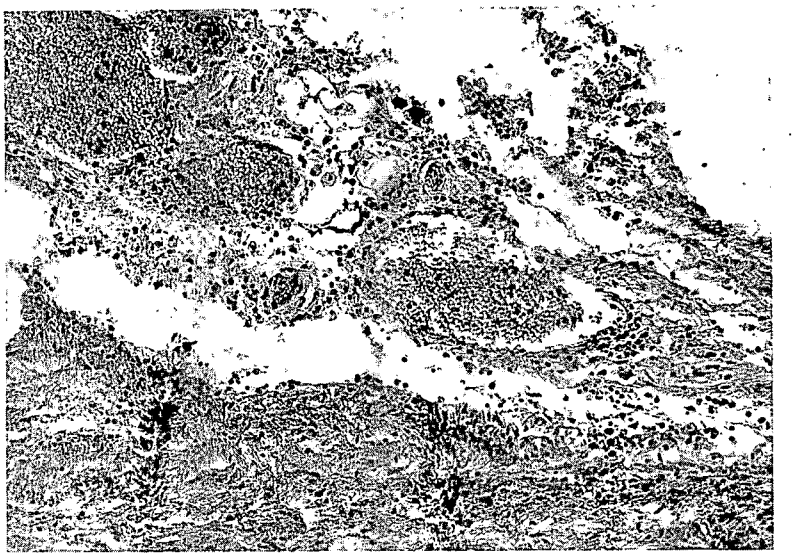

Fig. 1. Histological section of dura and spinal epidural space in a patient after continuous epidural anaesthesia (Table 1, patient 9) (HE-staining, magnification 216×). This patient developed severe bronchopneumonia whilst receiving epidural anaesthesia. Note the significant inflammatory reaction (invasion of lymphocytes, macrophages, and plasmocytes in dura and epidural tissue).

(Table 2, patient 2). All other findings in the control group were inconspicuous (Fig. 3).

Discussion

Spinal epidural infections and haematomas are rare complications of epidural anaesthesia;[7-9] but these occasionally occur spontaneously.[9-12] The need for a control group in the present study was evident, since risk factors (low-dose heparin, diabetes mellitus, bacterial infections) were present, which are known to increase the incidence of the spontaneous occurrence of these complications. The hyperaemia observed in both groups has to be considered as a part of the general hyperaemia which occurs when right ventricular failure is the cause of death.

Inflammatory reactions

The inflammatory alterations which were recorded in the majority of patients with epidural catheters may result from local irritation due to the catheter, or from the solutions injected into the epidural space. Animal studies indicate that they are primarily associated with the catheter itself.[13-15] These alterations probably have little clinical consequence since they occurred without significant symptoms or sequelae. The signs of bacterial infections in the

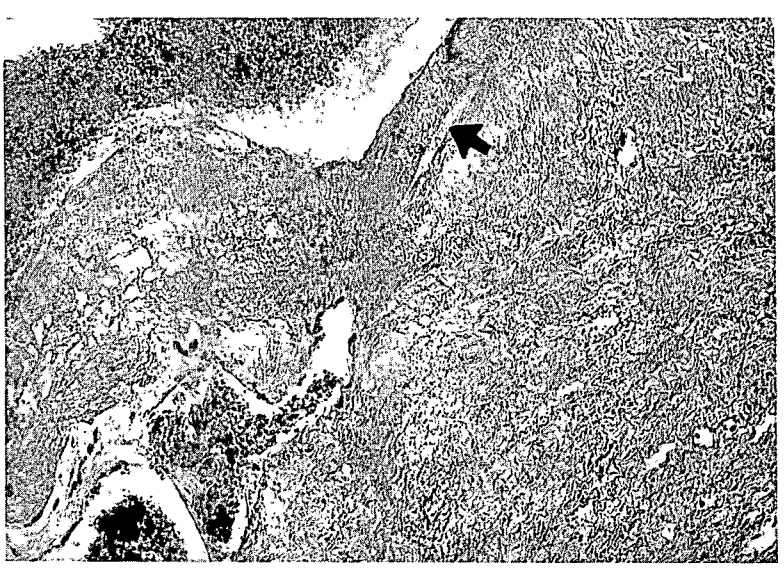

Fig. 2. Histological section of dura and spinal epidural space in a patient after continuous epidural anaesthesia (Table 1, patient 2) (HE-staining, magnification 216×). This patient developed significant thrombocytopenia whilst in receipt of the epidural. Note fibrin layers on the dura (arrow) and part of the epidural haematoma shown in the upper left-hand corner.

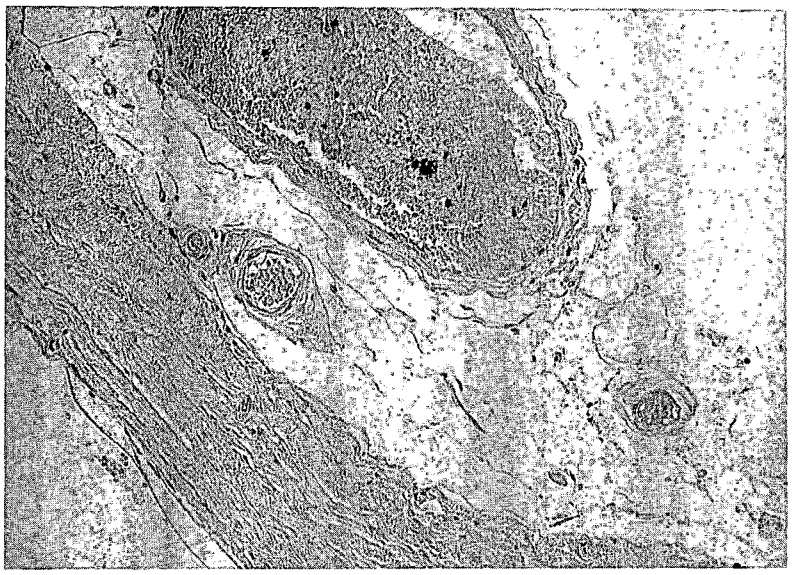

Fig. 3. Histological section of dura and spinal epidural space in a patient without epidural anaesthesia (Table 2, patient 6) (HE-staining, magnification 216×). This patient suffered from severe purulent peritonitis. There were no significant signs of inflammatory reactions.

epidural space, however, merit attention. The frequency of infectious complications as reported in the literature varies between 0.01% (abscess) and 20% (contamination), depending on the duration of the epidural block.[8,16,17] Several mechanisms that cause bacterial infection in the epidural space have been proposed. Infection may result from direct spread from osteomyelitis or discitis,[11,18] but this was not observed in our patients. Postmortem bacterial contamination is unlikely since the inflammatory tissue reactions indicated an *in vivo* pattern. Micro-organisms can be introduced by syringes, catheters, and drug solutions during performance of an epidural block.[16] Blood-borne infection or transmission via lymphatics from distant septic sources is also possible.[11] This mechanism is the most likely in the cases reported here, which is in accordance with Sollmann and coworkers.[19] Nevertheless, the epidural catheter is a foreign body and does serve as a possible location for the development of such infections. No such infections were observed in infected patients who did not receive epidural analgesia.

Spontaneous epidural infection is often associated with peripheral infections or minor trauma to the spine.[10] Haemorrhage in the epidural space caused by the insertion or movement of epidural catheters represents minor trauma which could possibly produce a locus for infection. It is tempting to suggest that there might be a link between epidural haemorrhage and epidural infections after epidural anaesthesia. Even mild epidural haemorrhage, as caused by a catheter, or an epidural blood patch, could be a precipitating factor for the development of epidural infection.[20]

Epidural haemorrhage

Epidural anaesthesia often leads to microtrauma with resultant small haemorrhages in the epidural tissue (Table 3). Usubiaga[9] found significant epidural haemorrhage at the time of laminectomy in 6% of patients who had continuous lumbar epidural anaesthesia for surgery of the spine. Blomberg and Olsson[21] reported epidural haemorrhage in patients after epiduroscopy. Microhaemorrhage results not only from catheter insertion,[22,23] but also from movement of inserted catheters.[24] However, the microhaemorrhages seem to cause only minor clinical impact in the majority of cases.

Various case reports of epidural haematomas have been published, but most of these occurred in patients on anticoagulants.[25–27] Nevertheless, many patients treated with low-dose heparin prophylaxis have received epidural anaesthesia without demonstrating symptoms of spinal haemorrhage.[28] It cannot be ruled out, of course, that low-dose heparin could have contributed to the minor epidural haemorrhages.

The epidural haematoma, however, which was observed in a patient with thrombocytopenia, was impressive. Thus it would be reasonable to assume that not only plasma coagulopathies but also thrombocytopenia and disorders of platelet aggregation[29–31] have to be considered as contraindications to epidural anaesthesia. The haematoma in question was only a few days old, so it probably developed from movement of an already inserted catheter, or during its removal, in this case 3 days before death. Therefore, if a patient with an epidural catheter in place develops a coagulation disorder, it should neither be used nor removed until coagulation is acceptable.

Tachyphylaxis

It is possible that these tissue changes may play a part in the development of tachyphylaxis to local anaesthetics during long-term epidural anaesthesia. The fibrotic sheet that forms around the catheter may prevent free distribution of injected solutions in the epidural space.[32] Haemorrhage and inflammatory reactions lead to changes in the epidural space that inhibit the spread of local anaesthetic solutions. This phenomenon may cause the higher incidence of failed blocks noted with serially repeated epidurals.[33] Previously performed epidural blood patches may interfere with the spread of local anaesthetics.[34,35] The thickening of the dura would also diminish passage of local anaesthetics into the subarachnoid space.

Conclusions

Our results support the reluctance of most anaesthetists to insert epidural catheters in the presence of systemic infection or immunoinsufficiency. Consideration should be given to discontinuing its use if infective complications develop in a patient who already has an epidural catheter in place. The strictest attention must be paid to aseptic conditions and antibiotic prophylaxis is strongly recommended if an epidural is deemed essential. A platelet count should be performed before catheter insertion in patients with a predisposition to thrombocytopenia, for instance cancer or pre-eclampsia, HELLP-syndrome.[36] The indications for an epidural should be carefully considered in patients with a thrombocytopenia. The epidural catheter should not be used or moved if coagulopathies develop. Patients with continuous epidural should always be closely monitored for signs of spinal pressure (back pain, pain on injection, local tenderness, fever, neurological deficits), since these may indicate spinal abscess or haematoma formation.

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A comparison of three methods of axillary brachial plexus anaesthesia

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Summary

One hundred patients scheduled for elective outpatient hand surgery had blockade of the axillary brachial plexus by one of three techniques; insertion of a catheter into the brachial plexus sheath (n = 25), use of paraesthesia (n = 50) or use of the nerve stimulator (n = 25) to localise the plexus. Only two patients required general anaesthesia for the planned surgery. Assessment of the dermatomes blocked did not demonstrate a statistical difference between the success rates of the three groups. The more nerves detected in the paraesthesia and the nerve stimulator groups before injection of local anaesthetic the higher the success rate of the block. We advocate use of the nerve stimulator technique in view of the possible risk of neurological damage associated with paraesthesia and the technical difficulties with the catheter technique, for routine brachial plexus blockade.

Key words

Anaesthetic techniques, regional; brachial plexus.

Axillary brachial plexus block is a safe and simple technique and is often recommended for these reasons. In particular, the minimal risk of pneumothorax means it is suitable for outpatient hand surgery. Many practitioners, however, admit that the method is less successful than approaches above the clavicle, which have less chance of producing total anaesthesia of the extremity.[1] This has led to the advocacy of various methods to improve the technique. Transarterial injection, the use of the nerve stimulator, eliciting paraesthesia, and increasing the volume of local anaesthetic are all suggested.[2–4] Few data exist that compare different approaches, but protagonists often claim high success rates for particular techniques.

Goldberg *et al.*[5] compared a single paraesthesia technique with a single electrical nerve stimulation and the transarterial approach. They concluded that the success rates and spread of block were no different. However, arterial puncture can result in arterial damage, haematoma formation, vascular insufficiency and inadvertent intravascular injection,[6–8] while paraesthesia can cause nerve damage.[9] For this reason, and the possible use of top-up injections or an infusion of local anaesthetic, the insertion of a catheter into the sheath is considered by some to be the method of choice.[10,11] We compared use of a catheter, a nerve stimulator with multiple nerve stimulations (avoiding arterial puncture and paraesthesia) and multiple nerve stimulations by paraesthesia, in a series of patients undergoing outpatient hand surgery.

Method

One hundred patients scheduled for outpatient hand surgery gave informed verbal consent and were then randomly allocated to receive one of the three techniques. Fifty patients were studied in the paraesthesia group, 25 in each of the other two groups. All of the blocks were performed or supervised by one of the two authors. All patients were unpremedicated and positioned on a trolley in the anaesthetic room. A cannula was inserted into the contralateral hand and full aseptic techniques were adopted. Lignocaine 1.5%, 40 ml with adrenaline 1:200 000 was used in each patient. No sedation or intravenous analgesia was used. The three techniques were performed as follows.

Catheter technique. The arm to be blocked was abducted to the horizontal position and the elbow flexed to 90°. An 18-gauge introducing needle from a B. Braun, Contiplex, Katheterset was inserted, after local skin infiltration, at the level of the insertion of pectoralis major at an angle of approximately 20–30° to the skin. The needle was aimed

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just superior to the axillary artery, until the neurovascular fascia was perforated, as indicated by a 'snap'. A 20-gauge catheter was then inserted to a depth of 4 cm from the point of entry into the neurovascular sheath. The introducing needle was withdrawn and the procedure repeated when the catheter failed to thread freely. The catheter was aspirated once sited and if negative for blood the arm was adducted and local anaesthetic injected whilst pressure was applied over the brachial plexus sheath below the site of catheter insertion.

Paraesthesia. The patient was positioned as for the catheter technique. The plexus was located at the level of the insertion of pectoralis major by searching for paraesthesia with a 22-gauge 3.8 cm regional block needle. Attempts were made to find up to three of the four main peripheral nerves. Local anaesthetic was injected in increments according to how many nerves were located. Pressure was applied over the lower part of the sheath during injection and the arm adducted after completion.

Nerve stimulator. A Bard Biomedical peripheral nerve stimulator (750 digital) and unsheathed block needle were used to identify up to three or four of the main branches of the brachial plexus by eliciting twitches in the relevant myotomes. Optimum nerve location was achieved by adjustment of the needle position so that stimulation was achieved with a current of less than 0.5 ma. The dose of local anaesthetic was injected in increments.

Assessment. Sensory and motor changes were assessed every 5 minutes for a period of 0.5 hours. Sensory loss was assessed with the blunt end of a 27-gauge dental needle and scored 0, no sensory loss; 1, loss of pinprick; 2, loss of touch. Sensory testing was carried out in the areas supplied by the axillary, musculocutaneous, radial, median and ulnar nerves, the medial cutaneous nerve of the forearm and medial cutaneous nerve of the arm. A block was deemed successful if three or more of the following nerves were blocked to an assessment score of 2 at 30 minutes: musculocutaneous, median, ulnar or radial. A failed block was one where only two or less of the above nerves were blocked to a sensory loss score of 2.

Results

Only two patients required general anaesthesia; all others were successfully managed with the block alone, with occasional use of peripheral nerve blocks. No intravenous sedation or analgesia was required.

The success rates of the three techniques used are shown in Table 1. There was no statistical difference in the number of successful blocks in the three groups (Chi-square, 5.733; degrees of freedom, 2). However, two patients required general anaesthesia in the catheter group because of complete failure of the block. These two and a further three in this group showed a pattern consistent with the catheter being anterior to and outside the sheath, that is blockade of medial cutaneous nerve of the arm, the forearm and the intercostobrachial nerve. Four patients in the paraesthesia and one in the nerve stimulator groups appeared to have completely failed blocks because of local anaesthetic outside the sheath. These figures are not significantly different.

The incidence of complete loss of sensation (score 2) in the four main cutaneous nerves with the three techniques is shown in Table 2. Our aim is to study the spread of local anaesthetic, so only those blocks in which there is evidence of the presence of local anaesthetic in the sheath are included. The catheter technique blocks the ulnar and median nerves significantly less frequently ($p < 0.01$) than the other techniques combined. The Fisher's exact test was applied because of the small numbers in the noninvolved groups, and combination of nerve stimulator and paraesthesia groups was thus undertaken. There was no significant difference between the three groups for blockade of the radial or musculocutaneous nerves (Chi-square, 0.371, degrees of freedom, 2; and 4.362, degrees of freedom, 2, respectively).

The number of nerves stimulated in each patient, either by paraesthesia or nerve stimulator, relative to overall block success rate is demonstrated in Table 3. There is a statistically significant greater chance of a successful block for the paraesthesia group if more than one nerve is

Table 1. A comparison of the success rates of the three techniques.

Technique	Paraesthesia $n = 50$	Nerve stimulator $n = 25$	Catheter $n = 25$
Age, years (SEM)	51.4 (2.28)	50.6 (3.64)	44.2 (3.56)
Weight, kg (SEM)	76.4 (1.36)	75.8 (1.71)	77.7 (2.10)
Success	41	18	14
Failed	9	7	11
% success	82%	72%	56%

Chi-square test not significant.

Table 2. Incidence of complete loss of sensation for the four main nerves.

	Radial nerve	Ulnar nerve	Median nerve	Musculocutaneous nerve
Paraesthesia	33/46 (72%)	46/46 (100%)	46/46 (100%)	27/46 (59%)
Nerve stimulator	16/24 (66%)	24/24 (100%)	24/24 (100%)	12/24 (50%)
Catheter	13/20 (65%)	15/20 (75%)	17/20 (85%)	16/20 (80%)

Table 3. Number of nerves detected compared with success of block.

	Number of nerves detected by paraesthesia ($n = 50$)		
	1 ($n = 10$)	2 ($n = 28$)	3 ($n = 12$)
Successful	6	23	12
Failed	4	5	0
% success	60%	82%	100%
	Number of nerves detected by nerve stimulator ($n = 25$)		
	1 ($n = 6$)	2 ($n = 15$)	3 ($n = 4$)
Successful	3	12	4
Failed	3	3	0
% success	50%	80%	100%

stimulated ($p < 0.05$). However, this just fails to reach significance for the nerve stimulator (Chi-square, 3.618; degrees of freedom, 2).

Table 4 shows the likelihood of a nerve block after the nerve's apparent stimulation in a particular patient. McNemars' statistical analysis was applied to paired results for individuals. There was no significant difference between the number of times that the nerve was apparently stimulated and the success rate of blockade of that nerve with the different techniques, apart from the stimulation of the radial nerve by paraesthesia: blockade of this nerve after its apparent stimulation by paraesthesia was significantly less likely to occur ($p < 0.05$).

The number of times nerves were blocked without apparent stimulation is shown in Table 5. The musculocutaneous and radial nerves were frequently blocked without stimulation.

Discussion

It is well known that techniques of brachial plexus blockade that involve paraesthesia may result in nerve damage[9] and that the transarterial approach can cause vascular injury.[6-8] The aim of our study was to compare paraesthesia with two nontraumatic techniques that involved neither paraesthesia nor passage through the artery. The techniques we used were based on our normal clinical practice. It was decided to study 50 subjects in the paraesthesia group since we wished to examine the efficacy of identifying differing numbers of nerves.

Our success rates of 82 and 72% for the paraesthesia and nerve-stimulator techniques respectively compare well with other workers,[4] but direct comparison is difficult in view of the different definitions of a successful block. We chose to define a successful block as one in which three of the major nerves are totally involved since this implies blockade of the plexus sufficient for surgery to proceed without further intervention. It must be pointed out that in all but two cases the surgery was able to proceed without recourse to general anaesthesia. No sedation was used in any patient.

There was no significant difference in our study between the three techniques with regard to success rate. Calculation of 95% confidence intervals, however, reveals that even though the measured difference in success between the paraesthesia and nerve stimulator groups is only 10%, this difference could be as much as 30%. The improved success rate may justify the minimal risk of nerve damage if this

Table 4. Number of patients in whom individual nerves were located by paraesthesia or nerve stimulator compared with success of nerve block.

Paraesthesia	Median	Ulnar	Radial	Musculocutaneous
Number of patients in whom nerve was located	44	37	12	4
Times blocked	42	36	7	3
Success rate	95%	97%	58%	75%
Nerve stimulator	Median	Ulnar	Radial	Musculocutaneous
Number of patients in whom nerve was located	22	12	8	4
Times blocked	21	12	5	0
Success rate	95%	100%	62%	0%

Table 5. Number of times nerve stimulated compared with number of times nerve blocked in all patients.

Nerve stimulated by paraesthesia ($n = 50$)	Median	Ulnar	Radial	Musculocutaneous
Number of times nerve stimulated	44	37	12	4
Number of times nerve blocked	46	46	33	27
% block without stimulation	< 1%	20%	63%	85%
Nerve stimulated by nerve stimulator ($n = 25$)	Median	Ulnar	Radial	Musculocutaneous
Number of times nerve stimulated	22	12	8	4
Number of times nerve blocked	24	24	16	12
% block without stimulation	< 1%	50%	50%	67%

were the case. It can also be seen that even though not significant the catheter technique appeared less successful and 20% of the time the catheter was outside the sheath.

This indicates that a 'click' and free threading of the catheter alone are not ideal determinants of localisation within the sheath on their own. This catheter failure rate may be reduced by the use of test doses with local anaesthetic or cold saline to confirm placement within the brachial plexus sheath.[12]

The more frequent failure to block the ulnar and median nerves in the catheter group may represent the higher spread of local anaesthetic; the catheter technique gave a picture similar to that expected for a supraclavicular approach. There also appeared to be an increased tendency to block the musculocutaneous nerve in the catheter approach, although not significant. The catheter technique in our study would thus be most beneficial for surgery on the upper arm, elbow and forearm.

The tendency, significant in the paraesthesia group, for a block to be more successful when several nerves are stimulated may indicate one or more of several options. Firstly, fractionation of the anaesthetic dose may result in an inappropriately low anaesthetic volume deposited in the sheath, if only one nerve is located. It is thus important to aim to stimulate the nerve appropriate to the surgical incision when fractionation of local anaesthetic is used, so that there is a good chance that the nerve will be blocked (Table 4). Secondly, it is still possible for the needle to be outside the sheath even after successful stimulation. Location of several nerves will increase the chance of entering the brachial sheath. Thirdly, spread of anaesthetic within the sheath may be hampered by fascial septa.[13] However, in the present study the ulnar, musculocutaneous and radial nerves are often blocked even though there was no evidence of stimulation of these nerves (Table 5). Other papers also confirm free spread of agents within the sheath and that the septa, though present, are not usually of clinical relevance.[4,14]

A technique that involves use of a nerve stimulator is a very real alternative to one that uses paraesthesia, with similar success rates and degrees of nerve involvement. The lower risk of nerve damage makes it a preferable technique. We found that in our study multiple injections were associated with an increased chance of whole plexus involvement, but in view of the risk of nerve and inadvertent vascular damage these injections should be limited to nerves that supply the dermatomes to be operated on. Large volumes of anaesthetic solution should be apportioned to these nerves and not small volumes scattered throughout. Insertion of a catheter by use of loss of resistance and ease of threading is not a simple technique and may result in some complete failures. Use of test doses may improve the success rate and this needs to be investigated further. The catheter technique does have the advantage that for long cases and for postoperative analgesia it can be topped-up or a continuous infusion may be used.[12]

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Propofol for long-term sedation in the intensive care unit*

A comparison with papaveretum and midazolam

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Summary

Thirty-seven patients with a wide range of illnesses were studied during mechanical ventilation of the lungs in an intensive care unit. Fifteen were sedated with a continuous propofol infusion, with analgesia provided by bolus doses of papaveretum. Twelve received a continuous infusion of papaveretum, supplemented by bolus doses of midazolam. The level of sedation was assessed every four hours and measurements were made of haemodynamic and respiratory variables. Levels of sedation were generally satisfactory in both groups. Six patients who received propofol required the use of muscle relaxants, because of their strong respiratory drives, to achieve synchronisation with the ventilator. There was no significant difference in respiratory or haemodynamic variables between the groups, but several patients required inotropic support because of their disease. There was no evidence of inhibition of adrenal steroidogenesis in the propofol group. Propofol can be a useful sedative agent in the intensive care unit, but sedative regimens should be tailored to individual patient requirements.

Key words

Anaesthetics, intravenous; propofol.
Intensive care.

Patients who require artificial ventilation of the lungs whilst in the intensive care unit invariably need some form of sedation for at least part of their stay. The ideal intravenous agent for use in this way would be short acting and noncumulative and thus allow rapid recovery for neurological assessment and early weaning from artificial ventilation. Such a drug should be free from adverse effects on the various organs of the body and not influence the metabolism of other drugs that might be used in these patients. The short acting intravenous anaesthetics Althesin and etomidate approached the ideal for this purpose and were extensively used, but unfortunately were withdrawn, the former because of an unacceptably high incidence of allergic reactions to its solubilising agent, and the latter because suppression of cortisol production was implicated in an increased mortality in severely injured patients.[1,2] The resultant gap was difficult to fill and most centres resorted to use of a benzodiazepine and an opioid. Initial pharmacokinetic studies with midazolam seemed to promise rapid recovery,[3] but there is growing evidence that it is not a suitable drug for use in the critically ill.[4,5]

Propofol is characterised by a short half-life[6] and initial studies on its use for short periods in the intensive care unit are very encouraging.[7,8] The present study was designed to assess the suitability of continuous infusions of propofol to provide sedation in patients for artificial ventilation in the intensive care unit and to compare it with the standard method in use in the unit, namely an infusion of papaveretum supplemented with bolus injections of midazolam.

Methods

The study was approved by the local ethics committee and the Committee on Safety of Medicines. Informed written consent was obtained from the patients, or when this was not possible because of their illness, from their next of kin.

*Propofol is not yet licensed for use by infusion in intensive care units in the United Kingdom and this study was carried out with a clinical trial certificate from the Committee on Safety of Medicines.

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Patient selection. Male or female patients aged 16–80 years who required mechanical ventilation of the lungs were admitted to the trial. Exclusion criteria were: known allergy to any of the trial drugs, pregnancy, patients who had undergone routine cardiac surgery, head injuries, those who had an established sedation regimen in the previous 24 hours and those with disorders of lipid metabolism. APACHE II scoring[9] was performed on all patients who were then randomly divided to receive either a propofol or papaveretum infusion.

Infusion regimens. An intravenous infusion of propofol was started at a rate of 1–3 mg/kg/hour, preceded by a bolus of 1.0 mg/kg if clinically indicated. The rate of infusion was adjusted to maintain a sedation level between 2 and 5 on the scoring system described by Ramsay and his colleagues,[10] although preferably at level 3. Intravenous bolus doses of papaveretum 2.5–5.0 mg were given to provide analgesia when required.

An infusion of papaveretum in the other group was started at a rate of 2.0 mg/hour and adjusted to maintain sedation at the required level. This was supplemented by intravenous boluses of midazolam 2.5–5.0 mg to achieve adequate sedation when necessary.

Neuromuscular relaxants were used in either group when it proved impossible to achieve synchronisation with the ventilator by other means.

Table 1. Details of patients with duration of sedation and ventilation and number of survivors.

	Propofol $n=15$	Papaveretum $n=12$
Male : female	4 : 11	6 : 6
Survivors	8	7
Age, years (SEM)	47.8 (3.7)	54.6 (5.9)
Weight, kg (SEM)	61.3 (3.8)	70.4 (4.4)
Height, cm (SEM)	162.4 (2.2)	167.6 (3.2)
Duration of ventilation, hours		
Mean (SEM)	101.6 (19.9)	66.6 (20.3)
Range	18.3–240	15–236
Duration of sedation, hours		
Mean (SEM)	84.5 (15.4)	66.9 (20.5)
Range	18–189	9.5–236

Table 2. Details of patients in propofol group.

Patient No.	Reason for admission to ICU	Concurrent disease	APACHE II score	Outcome
1	Acute tubular necrosis, ARDS	Paget's disease	34	Survived
2	Acute respiratory failure, pneumonia	Chronic granulocytic leukaemia; bone marrow transplant, immunosuppressed	15	Survived
3	Acute respiratory failure, pneumonia	Chronic granulocytic leukaemia, bone marrow transplant, pulmonary fibrosis, immunosuppressed	24	Died
4	Multiple trauma	None	13	Survived
5	Acute respiratory failure, asthma	Obesity, steroid therapy	10	Survived
6	Acute respiratory failure, asthma	Aortic valve replacement, steroid therapy	19	Survived
7	Acute respiratory failure, cytomegalovirus	Fibrosing alveolitis, immunosuppressed	22	Withdrawn, died
8	Postoperative emergency mitral valve replacement	None	24	Died
9	Acute respiratory failure, pneumonia	Acute myeloid leukaemia, bone marrow transplant, cytomegalovirus infection, immunosuppressed	22	Died
10	Postoperative peritonitis, pancreatitis	Subphrenic abscess, acute tubular necrosis	9	Survived
11	Acute respiratory failure, pneumonia, pneumocystis	Chronic granulocytic leukaemia, bone marrow transplant, immunosuppressed	14	Died
12	Acute respiratory failure, pneumonia	Polyarteritis nodosa, pneumocystis, immunosuppressed	17	Survived
13	Postrespiratory arrest, cerebral haemorrhage	Spinal cord tumour, renal transplant, fungal pneumonia, Parkinson's disease, immunosuppressed	17	Died
14	Post aortobifemoral graft	Asthma, diabetes, ischaemic heart disease,	15	Died
15	Postrespiratory arrest	Chronic renal failure, renal transplant, fungal pneumonia	18	Withdrawn, died

ARDS, adult respiratory distress syndrome.

Monitoring

Sedation. This was assessed every 4 hours using the Ramsay scale, while in addition one of the investigators assessed the quality of sedation every 24 hours on a four-point scale: excellent, good, adequate or poor. The nursing staff made a global assessment of the quality of sedation at the end of the study period and also the ease with which it was managed, again on a four-point scale, excellent, easy, adequate or poor. Patients who had received neuromuscular blocking drugs were scored at level 6.

The time taken to resumption of spontaneous ventilation and to obey a simple command was recorded at the end of treatment.

Cardiovascular. Heart rate, arterial and central venous pressures were continuously displayed and recorded every 4 hours. Cardiac output and pulmonary artery wedge pressure were measured if insertion of a pulmonary artery catheter was indicated.

Respiratory. Respiratory rate, minute volume, inspired oxygen concentration and arterial blood gases were noted every 4 hours. The alveolar–arterial oxygen tension difference ($A\text{-}aDo_2$) was also calculated at this time. The shunt fraction was measured in those in whom a pulmonary arterial catheter was inserted.

Biochemical. Cortisol levels were measured before the start of sedation and at 24 and 48 hours. The response to synacthen 250 μg intravenously was assessed at 30 and 60 minutes after the start of sedation and after 24 and 48 hours. Haemoglobin, packed cell volume, white cell and platelet counts, prothrombin time, urea and electrolytes, creatinine, albumin, aminotransferase and alkaline phosphates were measured before the start of sedation and also at 24 and 48 hours, but the results are not presented.

Statistical analysis

Statistical tests used were: analysis of variance, the paired and unpaired *t*-tests, the Mann–Whitney *U* test and the Chi-square test.

Results

Patient details. Twenty-seven patients were admitted to the trial, 15 of whom received propofol. Their anthropometric data are shown in Table 1; there was no significant difference between the groups in this respect. Eight patients in the propofol group survived, and seven who received papaveretum and midazolam, although one of the latter died 24 hours after leaving the intensive care unit. Three patients were withdrawn from the trial, two after propofol. The data from these patients, up to the time of their withdrawal from the trial, were included in the results. One of these latter was a 60-year-old man with fibrosing alveolitis who became hypotensive as the propofol dose was increased in an attempt to achieve synchronisation with the ventilator; the other was a 48-year-old woman in renal failure who developed lipaemia once parenteral nutrition was started. Sedation was stopped to allow neurological assessment in one patient in the control group and was never restarted.

The reasons for admission to the intensive care unit, the APACHE II scores on admission and the outcome for each patient are shown in Tables 2 and 3. There was no significant difference between the scores in the two groups

Table 3. Details of patients in papaveretum group.

Patient No.	Reason for admission to ICU	Concurrent disease	APACHE II score	Outcome
1	Acute respiratory failure	Chronic granulocytic leukaemia, pulmonary fibrosis, immunosuppressed	23	Survived
2	Acute respiratory failure, pulmonary oedema	Hypothyroidism, diabetes primary biliary cirrhosis	12	Survived
3	Peritonitis, acute respiratory failure	Chronic renal failure scleroderma, systemic lupus erythematosis, pulmonary fibrosis, immunosuppressed	29	Died 24 hours after leaving unit
4	Postcardiorespiratory arrest, pulmonary embolus	Aortobifemoral graft, atrial fibrillation	14	Died
5	Postlaparotomy for bleeding,			
6	Septic shock, fecal peritonitis	Ischaemic heart disease	23	Died
7	Pulmonary oedema	Caesarean section for placenta praevia, hysterectomy, massive transfusion	2	Survived
8	Postoperative partial hepatectomy	Carcinoid syndrome, massive transfusion	16	Survived
9	Multiple trauma, partial hepatectomy	None	7	Survived
10	Postoperative respiratory depression, hysterectomy	Gross obesity	15	Survived
11	Postoperative respiratory failure, aortobifemoral graft	Ischaemic heart disease	22	Died
12	Septic shock	Newly diagnosed severe hypothyroidism	16	Withdrawn, died

Table 4. Drug doses.

	Propofol group		Papaveretum group	
Dose of drug (mg)	Propofol	Papaveretum	Papaveretum	Midazolam
Total, mean (SEM)	7600 (2458)	55.0 (30.9)	433.5 (128)	14.2 (5.9)
range	263–36000	0–444	50–1200	0–75
mg/kg, (SEM)	128.8 (46.4)	0.86 (0.45)	6.3 (1.8)	0.2 (0.09)
range	5.8–720	0–64	0.7–18.1	0–1.13
mg/kg/hour, mean (SEM)	1.32 (0.24)	—	0.1 (0.013)	—
range	0.23–3.73		0.04–0.17	—

(Mann–Whitney *U* test). Multiple pathology was the rule rather than the exception in these patients.

Duration of ventilation. The durations of ventilation and sedation in the two groups are shown in Table 1. The propofol figures for time of ventilation exclude one patient who was initially weaned from ventilation, but her trachea was not extubated and she continued to receive intermittent mandatory ventilation for 2 months, and required virtually no sedation. The durations of ventilation and sedation were longer in those who received propofol, but the differences were not significant.

Drug doses. The doses of the drugs used are shown in Table 4. The mean total dose of papaveretum used in conjunction with propofol was 55 mg (range 0–444 mg). Relatively little midazolam was given to the papaveretum group, a mean of 14.2 mg, although one woman received 75 mg over a period of 120 hours.

Cardiorespiratory measurements. Inotropic support with dopamine or adrenaline was required in eight patients given propofol and five who received papaveretum in order to maintain haemodynamic measurements within normal limits. There were no significant differences from control within either group for any of the measurements, nor between the groups (Figs 1 and 2). Increase in sedative drug dose was associated with hypotension in five patients given propofol, one who was withdrawn from the trial (maximum infusion rate of propofol 33 mg/kg/hour), and in three who received papaveretum. Similarly, no differences in any of the respiratory measurements were seen between, or within, the two groups (Fig. 3).

Cortisol. The results of the cortisol measurements are shown in Table 5. Nine propofol patients and four papaveretum were already receiving steroid therapy on admission to the unit. The mean cortisol levels were high in the other patients, 1121 nmol/litre and 1169 nmol/litre for the propofol and papaveretum groups respectively. The results of the synacthen tests at 48 hours are also shown in Table 5. Four of the six patients given propofol who were not receiving steroids had short synacthen tests and all showed a positive response. Two of seven patients on steroids in this group also had a positive test, which was negative in the other five. Six of the seven patients in the papaveretum group who did not receive steroids on admission showed a positive result, while the other, a young man with multiple trauma, was negative; the one patient who received steroids and who was tested had no response to synacthen.

Assessment of sedation. The overall sedation scores are shown in Table 6. Patients were maintained between seda-

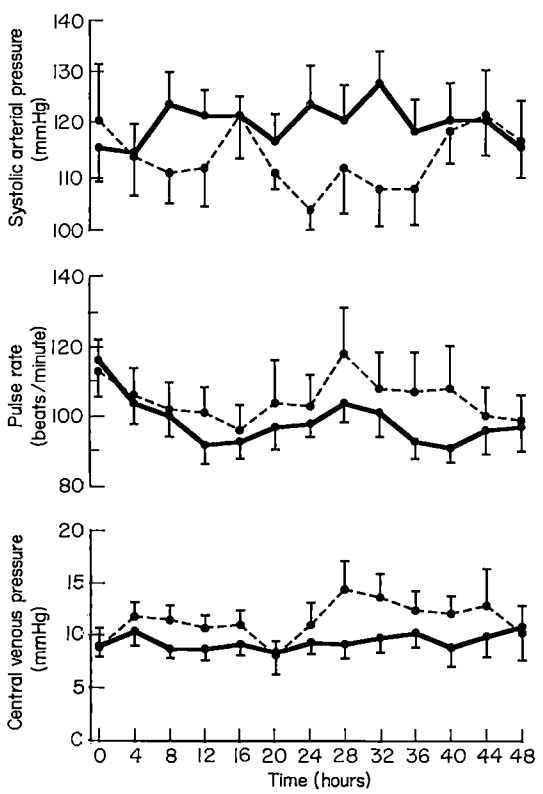

Fig. 1. Systolic arterial pressure, heart rate and central venous pressure during first 48 hours of sedation. ●...●, propofol; ●——●, papaveretum.

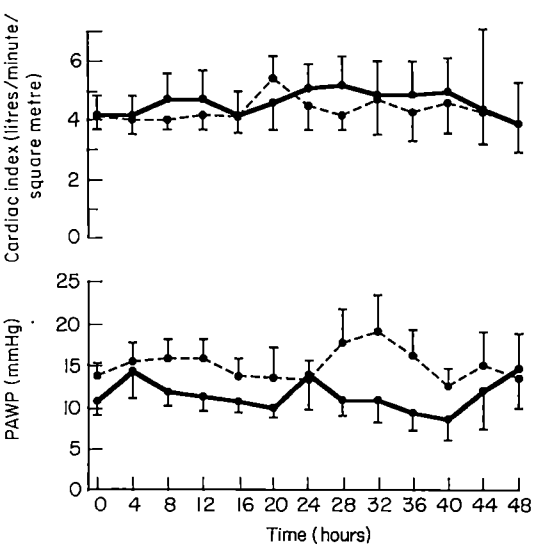

Fig. 2. Cardiac index and pulmonary artery wedge pressure during first 48 hours of sedation. ●...●, propofol; ●——●, papaveretum.

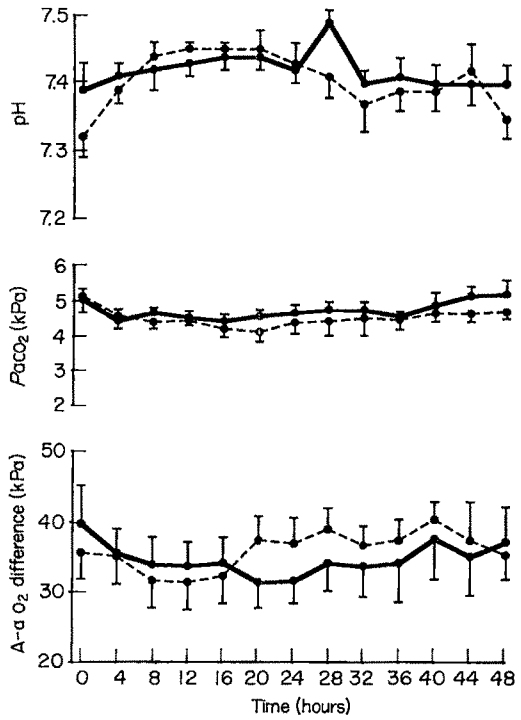

Fig. 3. pH, $Paco_2$ and A-aDo_2 during first 48 hours of sedation. ●...●, propofol; ●——●, papaveretum.

tion levels 2 and 5 for 80.8% of time in the propofol group and for 89.9% of the time in those who received papaveretum. The relatively high number of scores of 6 after propofol (14.1% of the time) is due to the assessment of paralysed patients. The time spent at sedation level 6 decreases to 1.5% and the time spent at the 2–5 levels increases to 92.6%, if these results are excluded, and these modified results are shown in Figure 4.

The global assessment of sedation by the investigators and nursing staff at 24 and 48 hours is shown in Table 7. The number of poor assessments in the propofol patients is again attributable to the use of neuromuscular blocking drugs.

Recovery. Eight propofol patients and seven papaveretum survived. The majority (four in both groups) were able to obey commands before cessation of sedation and were also able to breathe spontaneously before sedation was stopped. One of the four others in the propofol group was able to obey commands when the sedation was stopped, two 15 minutes after and one 2.5 hours after. One of the three who remained in the papaveretum group was able to obey commands 30 minutes after sedation was stopped, one 1.25 hours and the other 7.25 hours.

Table 6. Sedation scoring. Time spent (%) at each level.

Sedation level	Propofol	Papaveretum
1	5.1%	6.1%
2	28.8%	26.3%
3	13.5%	20.2%
4	23.1%	25.2%
5	15.4%	18.2%
6	14.1%	4.0%

Table 7. Global assessment of sedation.

	Propofol	Papaveretum
Nursing staff		
Overall management of patient		
Excellent	4	0
Easy	5	5
Adequate	3	6
Poor	3	1
Quality of sedation		
Excellent	4	0
Good	5	6
Adequate	2	6
Poor	4	0
Medical staff		
Excellent	4	1
Good	3	6
Adequate	4	5
Poor	4	0

Discussion

There are many factors involved in the provision of comfort for the patient in the intensive care unit and sedation may not always be beneficial.[11] In practice, however, most patients will not tolerate artificial ventilation and the intensive care environment without some form of sedation. The agent used should ideally be free from harmful short- and long-term side effects, be easy to manage, have inactive metabolites and be noncumulative. This would allow rapid recovery for neurological assessment when required. The most commonly used regimen in

Table 5.

	Propofol	Papaveretum
Number receiving steroids	9	4
Mean cortisol on admission in those patients not receiving steroids		
mean, nmol/litre (SEM)	1121 (547)	1629 (907)
range	547–2430	548–3110
Synacthen test		
Not receiving steroids	4+ve	6+ve 1−ve
Receiving steroids	2+ve 5−ve	1−ve
Not done	4	4

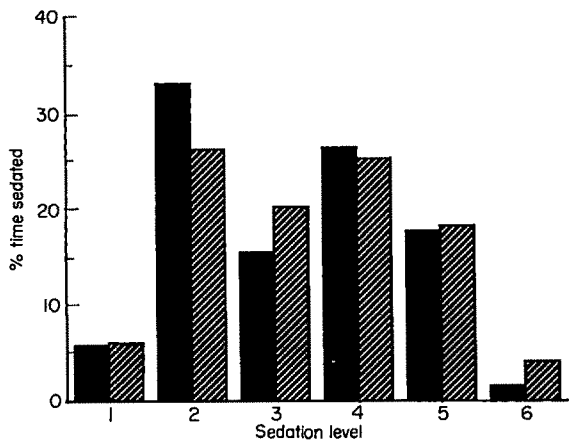

Fig. 4. Percentage of time spent at each sedation level excluding those patients who received neuromuscular blocking drugs. ■, propofol; ▨, papaveretum.

the United Kingdom is an infusion of opioids supplemented by a benzodiazepine,[12] but this has the disadvantage of relatively prolonged recovery, respiratory depression in spontaneously breathing patients and gastrointestinal stasis.

A previous study from this department[7] compared propofol with papaveretum and midazolam as the sedative regimens in postoperative cardiac surgical patients who required artificial ventilation and showed propofol to be the superior; these patients, however, represented a relatively homogeneous group. The present report illustrates many of the problems of comparative studies in patients in an intensive care unit. The multiple pathology and diversity of the clinical problems makes comparisons extremely difficult. All the patients were severely ill, which is reflected in the high mortality. Many of the patients required inotropic support because of their illness, so it is difficult to draw many conclusions from the measured cardiovascular data. Hypotension occurred in both groups, occasionally related to the administration of midazolam. There was a tendency for hypotension to occur more frequently in the propofol group; the one patient who was withdrawn from the study in this group for this reason was deliberately kept relatively hypovolaemic. The hypotensive effect of propofol is mainly the result of a decrease in systemic vascular resistance,[13] and in the present series where cardiac output was measured it was maintained. It is important that the circulating volume be maintained to minimise any decreases in arterial pressure when propofol is used to produce sedation.

Similarly, respiratory variables are adjusted to maintain values as near normal as possible. Respiratory depression during weaning was not a problem in either group in the survivors. Bolus doses of propofol are associated with quite marked respiratory depression,[14] although this is much less when it is used by infusion to produce light sleep.[15] Six patients in the propofol group (numbers 7, 9, 11, 12, 13 and 15, Table 2) required neuromuscular blocking drugs in order to control ventilation adequately, compared to none who received papaveretum and midazolam. The reason for the use of relaxants in this group and not in the other may be related to the individual pathologies of the six patients, five of whom were immunosuppressed and all of whom had strong respiratory drives. This may also be related, in retrospect, to inadequate use of papaveretum in these patients, with increased infusion rates of propofol in an attempt to deepen sedation to achieve synchronisation with the ventilator. Relatively small doses of midazolam were given in the other group, which reflects the policy in this unit to limit the use of benzodiazepines as far as possible.

The mean infusion rate of propofol used in these patients (1.32 mg/kg/hour) was higher than in our previous series in cardiac surgical patients,[7] although the latter had received high dose fentanyl anaesthesia. It will not be possible to recommend a standard infusion of propofol for sedation in the intensive care unit since it will depend, not only on the level of sedation required, but particularly on the condition of the patients and the nature of their pathology.[16] Thus young, previously healthy patients who require artificial ventilation for thoracic trauma will require considerably larger doses of sedative drugs than those who require ventilation for a short time after cardiac surgery.

The only incidence of adrenocortical suppression in a patient not already on steroids occurred in the control group. There is no evidence that midazolam causes depression of adrenal function.[17] Propofol only causes suppression of cortisol production at very high doses which are well outside the clinical range, and etomidate has been estimated to be 1500 times more potent in this respect.[18] No effect on adrenocortical function was shown after 8 hours propofol infusion[8] and this is confirmed for the more prolonged periods of infusion described here.

The objective assessment of sedation showed little difference between the two groups, although this was influenced by the number of patients who required relaxants. Nevertheless, the nursing staff and the investigators expressed a preference for propofol because it was so easy to manage, although this may reflect observer bias.

Sedation was achieved with either an infusion of propofol or midazolam; analgesia was provided with morphine in a multicentre trial which involved 100 patients admitted to the intensive care unit.[19] The majority of these patients were admitted after general surgery. The results were broadly similar to ours. The desired level of sedation was achieved easily in most patients in both groups. Duration of sedation was much shorter than in the present series (mean 20.2 hours in the propofol group compared to 84.5 hours) and the rate of propofol infusion slightly higher (1.77 mg/kg/hour compared to 1.32 mg/kg/hour). The authors found that propofol was a satisfactory agent for sedation in these critically ill patients.

Propofol is a very useful addition to the agents that can be used to provide sedation in the intensive care unit. Some patients did present management problems and it was not possible to achieve adequate synchronisation with the ventilator with propofol alone. The possibility that drug combinations may be superior to one drug alone in order to achieve optimum sedation in the intensive care unit must always be considered.

Acknowledgments

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Anaesthesia, 1990, Volume 45, pages 373–375

CASE REPORT

Recurrent bronchospasm during anaesthesia

C. S. MARTIN AND C. D. MILLER

Summary

Bronchospasm complicated several anaesthetics in a diabetic patient with chronic renal failure. The bronchospasm was accompanied frequently by bradycardia. The pathophysiology, treatment and implications for future anaesthetic management are discussed.

Key words

Anaesthesia; general.
Complications; bronchospasm.

Bronchospasm is a potentially life-threatening complication of anaesthesia. We describe a patient who developed severe bronchospasm on several occasions during anaesthesia.

Case history

A 26-year-old male insulin-dependent diabetic, who had developed renal failure which necessitated haemodialysis, presented for insertion of a dialysis cannula. He was hypertensive and had been treated for several years with atenolol. He was not allergic to any drugs. The pre-operative electrocardiograph (ECG) showed sinus rhythm at a rate of 65 beats/minute and left ventricular hypertrophy. There was no evidence of pulmonary oedema on auscultation of his chest or on inspection of the pre-operative chest X ray. He had been dialysed within the previous 24 hours and his serum potassium concentration was 4.3 mmol/litre.

He received his routine medication (including atenolol and nifedipine) before operation and a glucose and insulin infusion was started. He had undergone general anaesthesia on many occasions, but volunteered no history of anaesthetic complications. The available notes showed that he had undergone general anaesthesia on five occasions in the previous few months. Two anaesthetics were uneventful, but others were complicated by airway obstruction, bradycardia and ST segment depression.

Anaesthesia was induced with propofol 90 mg and atracurium 30 mg; the trachea was intubated, and the lungs were ventilated with nitrous oxide, oxygen and enflurane. Anaesthesia was maintained uneventfully for 55 minutes during which time the peak airway pressure was 2 kPa. Neuromuscular blockade was antagonised with neostigmine 2.5 mg and atropine 1.2 mg intravenously at the end of surgery and the lungs were ventilated with 100% oxygen. Initially the patient appeared to be breathing, since the abdominal wall was moving in a coordinated manner, but there was no movement of the chest wall or the reservoir bag. Manual inflation of the lungs was impossible and there was no air entry on auscultation. Obstruction of the tracheal tube was suspected and it was removed. The tube was normal and there was no evidence of excessive secretions. There was no tracheal deviation. Ventilation was attempted with a facemask and oropharyngeal airway but the lungs could not be inflated. The patient became cyanosed and his heart rate decreased from 110 beats/minute to 30 beats/minute. He was given atropine 0.6 mg intravenously and the heart rate increased to 90 beats/minute over the next 90 seconds. His condition improved rapidly and he started to breathe. His recovery was uneventful apart from slight wheeze on auscultation of his chest. There was no evidence of pneumothorax on the postoperative chest X ray.

The same anaesthetist provided anaesthesia for construction of an arteriovenous shunt one week later. The same anaesthetic agents were used but atropine and neostigmine were withheld and neuromuscular function, which was monitored, was allowed to recover spontaneously. A similar episode of severe bronchospasm occurred after extubation and resulted in hypoxaemia and bradycardia; both resolved after administration of atropine 1.2 mg.

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All previous medical records were obtained. These revealed that the patient had received 13 general anaesthetics in the previous 5 years. Five were complicated by cardiorespiratory problems. Two months previously he had been given a similar anaesthetic (methohexitone, atracurium, nitrous oxide, oxygen, isoflurane, morphine) for insertion of a dialysis line. Neuromuscular blockade was reversed with atropine 0.6 mg and neostigmine 1.25 mg; spontaneous ventilation began and pharyngeal secretions were aspirated. The tracheal tube was removed and sudden complete airway obstruction, cyanosis and a bradycardia of 20 beats/minute developed immediately. The anaesthetist gave atropine 0.6 mg and suxamethonium 100 mg, reintubated the trachea and started external cardiac massage. The condition of the patient improved rapidly and the trachea was extubated uneventfully a few minutes later.

Four days before that procedure, the patient was anaesthetised for incision and drainage of a neck abscess. Anaesthesia consisted of etomidate, fentanyl, atracurium, nitrous oxide, oxygen and enflurane. He developed marked ST segment depression on the ECG when the systolic arterial pressure decreased below 100 mmHg. Earlier that same month he presented for insertion of a dialysis cannula. Anaesthesia was induced with propofol and suxamethonium, after which the trachea was intubated with some difficulty. He developed a profound bradycardia during laryngeal instrumentation; this was treated successfully with intravenous atropine.

One year previously, during surgery for removal of a Tenckhoff catheter the anaesthetist noted that the patient 'had a very difficult airway due to bronchospasm, reversed by deepening anaesthesia'. Anaesthesia had been induced with propofol and suxamethonium and was maintained with nitrous oxide, enflurane and spontaneous ventilation. Two years earlier he had presented for construction of an arteriovenous fistula. Anaesthesia was induced with thiopentone and suxamethonium, the trachea was intubated and the lungs were ventilated easily with nitrous oxide, oxygen and halothane delivered by a Mapleson A breathing system. Muscle function returned and the abdominal wall moved as if the patient was breathing, but neither the chest wall nor the reservoir bag moved. The tracheal tube was replaced but there was no obvious obstruction and the diagnosis of bronchospasm was made. Anaesthesia was deepened and eventually spontaneous ventilation was established. Two further episodes of bronchospasm occurred during the course of the anaesthetic and were managed successfully by taking control of ventilation and deepening anaesthesia.

He had always received his normal medication (including atenolol) and a glucose and insulin infusion before anaesthesia. There was no difficulty in controlling his glucose or potassium in the peri-operative period.

Discussion

The particular features of this case are the severity and precipitancy of the bronchospasm, the accompanying bradycardia and the speed of recovery. The stimulus responsible for initiating bronchospasm may be of chemical, mechanical or neurogenic origin.[1] It is essential in the clinical setting to exclude obstruction of the tracheal tube or pneumothorax, neither of which occurred in this patient. There were no signs to suggest an allergic aetiology. This patient is not a typical asthmatic since he had no history of wheezing, cough, dyspnoea or other respiratory symptoms. He was a nonsmoker and had no positive findings on clinical examination of the respiratory tract. His pulmonary function showed a mild restrictive defect (FEV_1 2.35 litres, FVC 2.96 litres).

Beta-adrenergic blocking drugs may precipitate bronchoconstriction in asthmatics, but healthy volunteers, asthmatics in remission and patients who undergo general anaesthesia tolerate beta-blockade with little change in bronchomotor tone.[2-3] Cardioselective agents such as atenolol may precipitate bronchospasm but treatment with a selective $beta_2$-agonist is more effective than with a nonselective beta blocker.[4] Mechanical stimulation of receptors in the nose, larynx[5] or airways[6] may cause reflex bronchoconstriction and mucus secretion mediated by vagal efferent pathways.[7,8] These effects are characteristically of rapid onset and may also reverse rapidly. Such reflexes may be revealed by lightening the plane of anaesthesia, which happened on three occasions in this patient. The rapid recovery, lack of secretions and brisk response to atropine[9] suggest that vagally-mediated muscle contraction rather than mucosal oedema[10] gave rise to the clinical picture.

The bronchospasm occurred twice after the administration of neostigmine. There is a high density of muscarinic receptors in the smooth muscle of the large airways[11] and anticholinesterases can potentiate bronchospasm.[8] However, bronchospasm occurred in this patient both when neostigmine was given and when it had been withheld and it seems improbable that it was the cause of bronchospasm. Another feature of these episodes was bradycardia which accompanied the bronchospasm on three occasions, and on another occasion was associated with the insertion of an introducer into the trachea. Bradycardia may have been caused by hypoxaemia or instrumentation.

The incidents were treated by taking steps to maintain oxygen delivery. Bronchospasm resolved on two occasions after deepening anaesthesia with enflurane, which has bronchodilator properties. Autonomic neuropathy complicates long-standing diabetes[12] in 20–40% of patients[13,14] and this patient was investigated accordingly. Shortly after a period of haemodialysis (when he would be relatively hypovolaemic) he was placed supine on a tilting table and moved to vertical in 15° increments. Blood pressure, heart rate, ECG and plasma catecholamine concentrations were monitored during this manoeuvre. The responses were within normal limits. In addition, there was no history of postural hypotension, diarrhoea or delayed gastric emptying and he had a brisk response to atropine. These findings suggest there was no autonomic damage.[15]

Future anaesthetic management of this patient requires careful consideration. We plan to employ regional techniques where possible. He is on the urgent waiting list for cadaveric renal transplantation, for which spinal or epidural anaesthesia can be employed.[16] However, the patient has had two previous transplants and further surgery might result in profuse blood loss, a relative contraindication to regional blockade. Thus, general anaesthesia may be more appropriate. The management of the airway will influence any complications. Anaesthesia using a facemask would avoid mechanical stimulation of vagal receptors. Similarly, the laryngeal mask might be expected

to cause less autonomic stimulation than tracheal intubation.[17]

The minimum alveolar concentration required to obtund autonomic responses is greater than that required to ensure surgical anaesthesia.[18] Airway instrumentation activates these reflexes unless deeper planes of anaesthesia are employed. However, this may cause other problems in an anaemic, hypertensive patient.

Spontaneous recovery of neuromuscular function would avoid problems caused by neostigmine. Alternatively, anticholinergic drugs could be given before neostigmine, or in a higher dose. Edrophonium has fewer muscarinic effects.[19] Intravenous lignocaine has been used to decrease the incidence of coughing and laryngospasm associated with tracheal extubation.[20] Atracurium and vecuronium are useful in renal failure, but are less vagolytic than other muscle relaxants. Beta-blockade may unmask vagal effects, and consequently an anticholinergic agent will be given prophylactically.

The potentially fatal complications of anaesthesia in this patient appear to be due to exaggerated vagal responses to mechanical airway stimulation. Our plan for a subsequent general anaesthetic includes the use of intravenous glycopyrronium before induction of anaesthesia, and a further dose before tracheal extubation. Neuromuscular blockade will be monitored and allowed to recover spontaneously if controlled ventilation is required. If reversal were required, we would administer a small dose of neostigmine with an increased dose of glycopyrronium, as is recommended for patients on beta blockers.[21]

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CASE REPORT

Meningitis after obstetric spinal anaesthesia

S. P. ROBERTS AND H. V. PETTS

Summary

A case of meningitis after obstetric spinal anaesthesia is reported. The possible aetiological causes of postspinal meningitis are discussed and the difficulty in differentiation between aseptic and bacterial meningitis noted. Ways to reduce the risk of bacterial contamination of cerebrospinal fluid are mentioned. The patient in this case made a full recovery, but the use of spinal anaesthesia in these patients is open to question.

Key words

Anaesthetic techniques, regional; spinal.
Complications; infection.

Meningitis after lumbar puncture and spinal anaesthesia is an extremely rare but nonetheless very serious complication. There is much discussion about the aetiology and prognosis of this condition. Such a patient is reported here.

Case history

A 28-year-old para 1 female, whose first pregnancy and antenatal history were unremarkable, was admitted in labour. Her cervix reached full dilatation 1 hour and 15 minutes after admission and she delivered a healthy baby 20 minutes later. The placenta, however, was retained and the patient requested regional anaesthesia for manual removal. She was apyrexial immediately after delivery.

Spinal anaesthesia was performed in the sitting position after the skin had been prepared with chlorhexidine and alcohol. A standard pack with disposable needles and syringes was used. After initial failure to perform a lumbar puncture with a 26-gauge needle an introducer was employed and the needle inserted to produce a clear tap. Hyperbaric bupivacaine, 2.5 ml was injected and produced a block up to T_7. Her cardiovascular system remained stable and an intact placenta was removed.

The next morning she was mobilised, but at 1400 hours (approximately 18 hours after the procedure) she developed a severe frontal headache, worse on sitting, photophobia and shivering with a pyrexia of 38°C. At 2000 hours her temperature had increased to 39.6°C and she complained of marked photophobia. Her white cell count at this time was 19.8×10^9 litres and blood cultures were negative. She was treated with cephradine and metronidazole because the initial presumptive diagnosis was postdelivery sepsis and a low pressure type spinal headache. Eighteen hours later she developed a marked positive Kernig's sign and a left quadriceps weakness. Her temperature at this time was 37.4°C.

Lumbar puncture was performed and revealed turbid cerebrospinal fluid (CSF) at a pressure of 230 mm H_2O. This contained 6.64×10^9 polymorphonuclear leucocytes/litre and 1.25×10^9 red cells/litre. The glucose was 1.2 mmol/litre (normal 2.8–4.0) and protein 3.25 g/litre (normal 0.1–0.4). No bacteria were seen on Gram staining nor were any grown on culture. A diagnosis of either a partially treated bacterial meningitis or a chemical meningitis was made. She was treated with ceftazidime and flucloxacillin for 7 days and made an uneventful recovery. She was discharged home with no residual neurological deficit.

Discussion

The aetiology of meningitis after lumbar puncture and spinal or epidural anaesthesia is very debatable. The causes include aseptic meningitis from disinfectants and detergents,[1] the introduction of bacteria from the bloodstream of a septicaemic patient,[2] introduction of foreign material due to coring,[3] the use of certain local anaesthetic solutions,[4] and even coincidental intercurrent viral infection.[5]

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It is important to attempt to explain the aetiology of the individual case, despite the reassurance of Dripps and Vandam's study[6] which failed to show any significant serious long-term neurological sequelae after spinal anaesthesia, otherwise repetition of the problem may occur, as in the series reported by Goldman and Sandford.[1]

Brandus[3] studied the incidence of coring with re-usable 22-gauge needles. Fragments of skin and iodine were found in 75% of needles inserted with their stylets which were withdrawn without performing a dural puncture. No material was found on the tips of needles after successful dural puncture; this was said to be because the needle tip was flushed during the test aspiration. It would seem from other studies that the incidence of coring is reduced with the use of well-fitting stylets or introducers. It is suggested that certain anaesthetics cause postepidural meningitis, for instance heavy amethocaine, which contains polyvinyl pyrollidine, caused meningitic symptoms after epidural anaesthesia.[4] Intercurrent viral meningitis after epidural anaesthesia has been described by Neumark *et al.*[5] The onset was gradual in this case; it occurred 7 days after the spinal and the Cocksackie B virus was the causative agent. The results of lumbar puncture, clear CSF with a low cell count, were typical of a viral meningitis.

Most causes of aseptic meningitis are attributed to detergent contamination of syringes and other equipment, either re-usable[1,7] or disposable.[8] Goldman and Sanford[1] describe five cases, four of which followed a similar clinical pattern. The patient developed a marked pyrexia (mean 39.7°C) and meningitic symptoms about 11 hours after spinal anaesthesia, although onset varied from 5 hours to 2 days. The CSF pressures on lumbar puncture varied from 140–300 mmHg and the white cell count was between 2.6×10^9 and 27.0×10^9/litre; 90% were polymorphonuclear cells. The CSF sugar varied between 2 and 4 mmol/litre. Smears and cultures were negative. The peripheral white cell counts were elevated in these patients and the pyrexia settled in 72 hours (usually less than 48 hours). It is difficult therefore to differentiate between bacterial meningitis and aseptic meningitis on the grounds of lumbar puncture alone, which explains why most of these cases are treated with aggressive antibacterial therapy.

Berman *et al.*[2] describe another possible cause of meningitis after spinal anaesthesia. An unusual Group D streptococcus was cultured from the CSF of a patient after meningitis, which developed after a spinal anaesthetic for removal of renal calculi. It was suggested that lumbar puncture can create a site of low resistance to infection across the blood/brain barrier, to allow infection to cross into the CSF.

It is important, whatever the aetiology of postspinal meningitis, that steps are taken to minimise the risk of this rare complication. Phillips[8] discusses the preparation and sterilisation of equipment before lumbar puncture. Brandus[3] found that 30% of needles, supposedly ready for use on nondisposable spinal trays, contained blood corpuscles or pieces of tissue. This may mean that only disposable needles and introducers should be used. Similarly, disposable syringes are less likely to contain contaminants than the re-usable variety.

The anaesthetist relies on the manufacturer of disposable syringes and drugs to ensure freedom from contaminants, and skin preparations should be performed using a coloured preparation. Betadine is probably better than chlorhexidine in this respect. It is advisable to use an introducer to prevent skin contamination of the needle tip. However, if this is done it is only likely to be effective if the introducer contains a stylet, otherwise the spinal needle will be inserted through the core of skin, negating its effectiveness. Phillips[8] recommends the use of gloves, but the use of gowns and masks remains debatable.

It may be, in view of the case described by Berman and Eisele,[2] that bacteraemia or the risk of bacteraemia represents a relative contraindication to spinal anaesthesia. The incidence of bacteraemia after uncomplicated normal delivery varies between studies, but rates of 3.6%[9] to 7.2%[10] have been reported. However, if manipulation of the uterus is performed the incidence may be much higher; Ritvo *et al.*[11] quote 85% after suction termination of pregnancy, and it may be that manipulation of the retained placenta causes a high bacteraemia rate.

It is difficult, in this individual case, to determine whether the lumbar puncture results show a picture of aseptic meningitis or a partially treated bacterial meningitis. If this case was the result of post-bacteraemic introduction of bacteria into the CSF via the lumbar puncture site, then this suggests that spinal anaesthesia should be used with caution for the removal of retained placenta and should not be used if bacteraemia is suspected or the patient is pyrexial.

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Anaesthesia, 1990, Volume 45, pages 378–380

CASE REPORT

Spinal anaesthesia in a child with Job's syndrome, pneumatoceles and empyema

J. B. TAPPER AND A. H. GIESECKE

Summary

We present a case of acute bowel obstruction in an immunocompromised child, who also had lobar pneumonia and a giant unilateral pneumatocele. She was successfully managed with subarachnoid anaesthesia for exploratory laparotomy to relieve a colonic obstruction. This proved to be a safe alternative to general anaesthesia with tracheal intubation in this patient and should be considered in infants and children in selected cases whenever a contraindication to general anaesthesia exists.

Key words

Complications; Job's syndrome.
Anaesthetic techniques, regional; spinal.

Job's syndrome is an immunological disorder of unknown aetiology characterised by overproduction of IgE and by neutrophil or monocyte chemotactic deficits. Patients demonstrate recurrent bacterial infections of the skin, sinuses and pulmonary tract that begin in early childhood. Less common clinical signs include coarse facies, chronic eczemoid eruptions, 'cold' cutaneous abscesses and mucocutaneous candidiasis.[1,2]

We report the use of subarachnoid anaesthesia for exploratory laparotomy in a child with Job's syndrome, whose clinical course was complicated by left pneumatocele and right lobar pneumonia. We are unaware of any reports of other such patients managed in this way.

Case history

A 16-month-old, 9.1-kg black female presented to the emergency room with a 24-hour history of fever and respiratory distress. She had a significant past history of numerous infections which included methicillin-resistant *Staphylococcus aureus*, cutaneous abscesses and recurrent *Staphylococcus aureus* pneumonia. The later episodes resulted in multiple large left lung pneumatoceles. A barium swallow demonstrated severe gastro-oesophageal reflux during the most recent admission for pneumonia. A simple gastrostomy was performed at that time under local anaesthesia. An admission chest X ray revealed a large right pleural effusion which subsequently yielded gram-positive cocci in clusters. Therapy was initiated empirically with intravenous ceftazidime and vancomycin.

The patient's condition gradually improved until the 9th day in hospital when she developed severe abdominal distension. This led to further respiratory embarrassment and displacement of the gastrostomy tube. A barium enema indicated a colocolonic intussusception at the splenic flexure, which failed to reduce during a second barium examination. She was therefore scheduled for an emergency exploratory laparotomy.

Physical examination before operation revealed a thin, tachypnoeic child, whose vital signs were arterial blood pressure 95/55 mmHg, pulse rate 145/minute, breathing 52/minute, and rectal temperature 38°C. Pulse oximetry revealed an O_2 saturation of 96% whilst breathing oxygen 4 litres/minute via nasal cannulae. Auscultation of the lungs revealed reduced breath sounds in both lower lung fields, coarse rhonchi and dullness to percussion in the right base. A 12 French gauge thoracostomy tube draining the right hemithorax was in good position. The abdomen was distended and bowel sounds were decreased.

Laboratory values before operation included: haemoglobin 9.9 g/d litre, haematocrit 30%, white blood cells 18 000/cu mm, platelets 240 000/cu mm. Arterial blood gas analysis whilst breathing air revealed: pH 7.45, $Paco_2$ 5.2 kPa, Pao_2 7.6 kPa. Chest radiography demonstrated right, middle and lower lobe opacification, with multiple pneumatoceles in the lower and middle left lung fields.

She was brought to the operating theatre where an ECG, Dinamap, precordial stethoscope and pulse oximeter were applied and the patient was given intravenous ketamine 2.0 mg incrementally until sedated. A subarachnoid block was

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then performed in the left lateral position at the L_{3-4} interspace using a 22-gauge 1.5-inch Quincke needle. The anaesthetic solution consisted of amethocaine 1% made hyperbaric with an equal volume of 10% dextrose solution to which adrenaline 20 μg had been added. A total of 1 ml (5 mg or 0.55 mg/kg) was injected. Motor block of the lower extremities was observed in just over 2 minutes. A T_4 sensory level was obtained 6 minutes after injection, as tested using a peripheral nerve stimulator set at 100 Hz. We observed no significant changes in heart rate or arterial blood pressure.

Soft restraints were applied to the upper extremities, an infusion was started in the right foot with a 20-gauge cannula and ketamine was titrated in 0.5-mg increments as needed for sedation.

Exploratory laparotomy revealed an impacted transverse colon. The patient remained haemodynamically stable throughout the 55-minute open colonic disimpaction and gastrostomy revision. She continued to receive O_2 4 litres/minute by nasal cannulae, and the O_2 saturation remained at 96–98%. She was awake and alert at the end of surgery after receiving a total of 18 mg ketamine (2 mg/kg) over 75 minutes. A T_4 sensory level was still present 99 minutes after subarachnoid injection. Recession of the motor block, as evidenced by spontaneous movement of feet and toes, was noted 4.5 hours after block placement.

The patient showed no evidence of complications attributable to the anaesthetic technique at 24, 48, and 72 hours after anaesthesia. Her postoperative course was complicated by recurrence of pneumothorax and re-accumulation of a pleural effusion. She was discharged to the care of her parents in good condition 38 days after surgery.

Discussion

Patients with Job's syndrome often suffer recurrent, severe pulmonary infections with *Staphylococcus aureus*.[1,2] Acute staphylococcal bronchopneumonia in children has a tendency to produce rapid multilobar consolidation, with subsequent giant pneumatocele formation which may simulate a pneumothorax.[3,4] The incidence of empyema is over 90%.[3]

We chose to avoid general anaesthesia with tracheal intubation in this patient in order to prevent the hazards of positive pressure ventilation, which might result in air trapping, rupture of the pneumatocele and possible formation of a tension pneumothorax or a bronchopleural fistula. A series of events such as these would have reduced the ability to ventilate the left lung, even after chest tube placement. Generally, if this were to occur, the contralateral mainstem bronchus would be selectively intubated. However, the presence of a right-sided bronchopneumonia made bronchial intubation a less attractive option because of the large ventilation/perfusion mismatch presumably present on that side.

Other anaesthetic choices for this patient included lumbar or thoracic epidural block; however, our experience with these techniques in children was limited. Caudal blocks are safe and technically easy in children. Unfortunately, potentially toxic doses of local anaesthetics are needed to achieve a high thoracic sensory level. The safest anaesthetic in this patient appeared to be a subarachnoid block. In infants and children this is technically easy, uses a small dose of local anaesthetic and provides a reliably dense sensory, as well as motor, blockade.

Spinal anaesthesia has been used for major abdominal surgery in children for many years. Tyrell Gray[5] in 1910, reported over 300 spinal anaesthetics performed for abdominal or lower extremity procedures with only a single death. This represented a strikingly low mortality at a time when the administration of open drop chloroform was the anaesthetic of choice for children. Berkowitz and Greene[6] published a series of 350 spinal anaesthetics in children under 13 years of age which included 307 cases of appendicitis and five intestinal obstructions. There were no fatalities and they reported no morbidity attributable to their anaesthetic technique. Abajian *et al.*[7] in 1984, re-introduced the use of spinal anaesthesia as a safe alternative to general tracheal anaesthesia in selected high-risk infants. They performed 81 spinal anaesthetics in 78 infants. Vasoactive agents were not needed to maintain cardiovascular stability, and there were no episodes of hypotension or bradycardia despite the omission of a fluid preload. In addition, no major intra-operative or postoperative complications occurred.

Children less than 5 years of age remain haemodynamically stable despite a virtually complete preganglionic sympathetic block. Dohi *et al.*[8] suggest that this may be due to an underdeveloped sympathetic nervous system, or perhaps a relatively smaller percent of the total blood volume present in the lower extremities. Motor block after subarachnoid anaesthesia has a significantly faster onset in children, and recovery is more rapid. Rice[10] believes that this may be due to age-related differences in the quantity of cerebrospinal fluid (CSF), as well as the total surface area of the spinal cord and nerve roots. In addition the rate of absorption of local anaesthetics also may differ considerably from that of the adult.

Hyperbaric amethocaine is currently the agent of choice for spinal anaesthesia in infants. However, the dose response relationship of subarachnoid amethocaine has not been studied in this age group. Published studies in infants less than one year of age have employed doses of amethocaine that ranged from 0.22 mg/kg to 0.65 mg/kg; younger infants required larger doses.[6,7,9] These doses appear to be large when bodyweight is used as a frame of reference, but are quite modest when the concentration of amethocaine per ml of CSF is considered (CSF volumes are 4–6 ml/kg in infants less than one year and 2 ml/kg in the adult). Rice obtained consistent T_4 sensory level and a duration of motor block that averaged 125 minutes, with 0.4 mg/kg amethocaine with 20 μg adrenaline.[10] The duration of surgical anaesthesia is somewhat shorter and averaged 70–90 minutes. Increasing the dose of amethocaine prolongs the duration of both the motor and sensory block (the ultimate sensory level is more dependent on the position of the patient). Our patient had a prolonged motor block which was even greater than had been anticipated by the addition of adrenaline.

A subarachnoid block appeared to be the safest anaesthetic alternative, but we recognised its potential for life-threatening complications. It is obvious that the loss of intercostal muscle function could lead to further respiratory embarrassment when abdominal distension is present. In addition, the sympathetic blockade associated with subarachnoid anaesthesia could theoretically increase the risk of colonic perforation from unopposed parasympa-

thetic stimulation of an obstructed bowel.[11] The risk of meningitis or an epidural abscess after lumbar puncture in a febrile patient has also to be considered. There have been isolated reports of meningitis in bacteraemic patients and a single case report of an epidural abscess after a spinal anaesthetic, although the chances of the occurrence of this complication are minimal. A series of 65 667 and 78 746 consecutive spinal anaesthetics have failed to produce a single pyogenic complication.[12–15]

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Anaesthesia, 1990, Volume 45, pages 381–382

CASE REPORT

Forty-eight single-shot epidural injections on the same patient

G. A. KATSAROS, G. P. HANDJIS AND J. ANASTASIADES

Summary

A patient is described who has received 48 single-shot epidurals with plain lignocaine. No complications were encountered at any time. Nuclear magnetic resonance imaging confirmed that no dural damage had occurred.

Key words

Anaesthetic techniques, regional; epidural.

Repeated epidural injections are usually for administration of top-up doses via an epidural catheter. We report here a patient who required multiple anaesthetics and in whom repeated single shot epidural injections were used.

Case history

The patient was a 36-year-old male with a stricture of the sigmoid colon which was caused by an overdose of ergotamine used to treat his migraine. Treatment for the stricture was repeated dilatations via a colonoscope.

General anaesthesia was used initially, but this was changed to a caudal block. However, the sacral hiatus was difficult to locate and compounded by the fact that the patient gradually put on weight. This was therefore changed to a lumbar epidural block which was performed on each occasion at the L_{4-5} level using the loss of resistance technique and 12 ml plain 1.5% lignocaine injected; this was sufficient to allow the dilatation to be performed and always produced a sensory block to T_{12}. The procedure was repeated every other week for 2.5 years and at the moment is performed every 20 days. To date he has received 48 epidural injections.

No difficulty has been encountered in performing the blocks and there has been no evidence of any complications. It was decided, in view of the large number of blocks, to perform magnetic resonance imaging after the 48th epidural to assess the integrity of the ligaments and meninges in the lumbar and caudal regions. The results are shown in Figures 1–3, which demonstrate normal anatomy in the region.

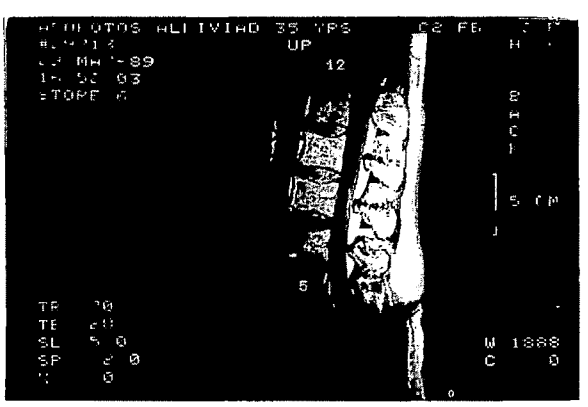

Fig. 1. Magnetic resonance imaging of longitudinal section of lumbar spine. The lumbar vertebrae are numbered. There is no evidence of meningeal damage.

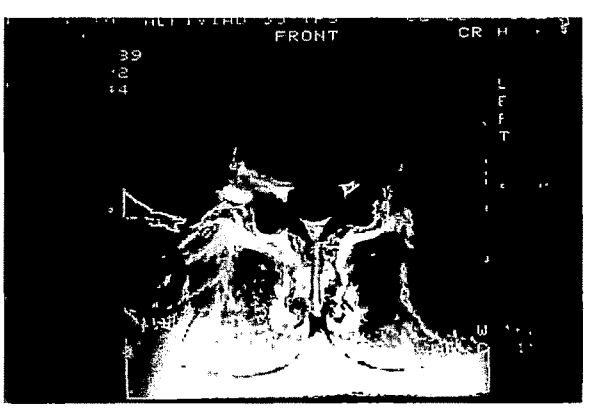

Fig. 2. Cross-section of spine at L_5 level. There is no evidence of meningeal damage.

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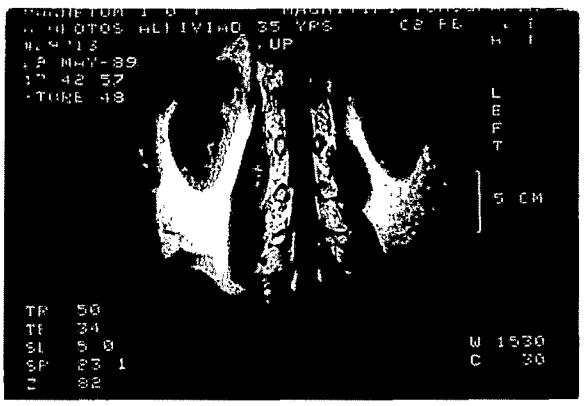

Fig. 3. Anteroposterior section of lumbar region. There is no evidence of meningeal damage.

Discussion

To our knowledge, there has been no report of such a large number of epidural blocks performed on a single patient, although repeated injections through chronically implanted catheters are now commonplace in the management of intractable pain. The time interval between anaesthesia requirements was 2 weeks in our patient, which we considered did not justify insertion of an epidural catheter. Initially we tried the caudal approach, but identification of the landmarks became increasingly difficult. In addition, on two occasions there was some evidence of intravascular injection of the local anaesthetic.

There is no evidence available to indicate how often epidural injections can be performed safely. It was thought initially that the incidence of complications might increase with increasing number of blocks, but this has not been so; indeed, no complications have been encountered. No difference has been noted in the 'feel' of the ligaments to the advancing needle. The integrity of the anatomy of the region has been confirmed by magnetic resonance imaging. No evidence of any diminution in the effectiveness of lignocaine has been found.

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CASE REPORT

Anaesthesia for the treatment of a giant cerebral aneurysm under hypothermic circulatory arrest

A. N. THOMAS, J. M. ANDERTON AND N. J. N. HARPER

Summary

The anaesthetic management of a patient whose giant cerebral aneurysm was clipped is described. Profound hypothermia and thiopentone were used to provide cerebral protection during circulatory arrest. Atracurium was used to provide muscle relaxation; the level of neuromuscular block and plasma concentrations of atracurium and laudanosine were measured.

Key words

Cerebral aneurysm; cerebral protection, atracurium.
Circulatory arrest; cardiopulmonary bypass.

A giant cerebral aneurysm presents great technical difficulties because of size and lack of a definitive neck. It is necessary, in order to overcome difficulties with a slack aneurysm, to provide a bloodless field that will not bleed if incised. These conditions can be met using the technique of complete circulatory arrest which may allow otherwise inoperable aneurysms to be clipped. This case report describes the anaesthetic management of a patient in whom this technique was used to permit the clipping of a giant middle cerebral aneurysm.

Case history

A 30-year-old woman, who weighed 47 kg, presented with repeated grand-mal convulsions and right-sided weakness. This developed 3 hours after the birth of her fourth child. Her previous medical history was unremarkable except for development of a transient, severe parieto-occipital headache and right-sided facial weakness after the birth of her first child. She was drowsy on examination, had a mild right-sided weakness and generalised hypertonia. A CT scan demonstrated a left temporal lobe intracerebral haematoma. There was an area of ring calcification in the left middle trifurcation and these appearances suggested a long standing, partly calcified aneurysm that had ruptured. This was subsequently confirmed at angiography. Figure 1 shows one of the views of the aneurysm during the procedure.

The patient presented for surgery 25 days after her initial haemorrhage; her general condition had remained stable. She was premedicated with temazepam 20 mg and arrived in the anaesthetic room calm but responsive. Additional sedation was given with midazolam 4 mg; 16-G cannulae were sited in both arms and radial artery pressure monitoring established. Silver/silver chloride electrodes were then positioned to obtain the electromyographic response of the *adductor pollicis* with the use of the Datex Relaxograph. The patient breathed added oxygen during this time. Anaesthesia was induced with fentanyl 250 μg followed by thiopentone 100 mg. The Relaxograph was then calibrated and muscle relaxation facilitated with atracurium 40 mg. The patient was positioned with 10° head-up tilt to facilitate venous drainage and to avoid pooling of blood in the cerebral vessels during circulatory standstill.

A pulmonary artery flotation catheter was introduced via the internal jugular vein and nasopharyngeal, oesophageal and peripheral temperature monitoring was established. An atracurium infusion was commenced; the rate was adjusted to maintain 95–100% block, as measured by the Relaxograph. Blood was obtained for subsequent estimation of plasma atracurium and laudanosine concentrations using the method described by Simmonds.[1] The results of these estimations are shown in Table 1. Anaesthesia was maintained with isoflurane in oxygen-enriched air and boluses of fentanyl as required. This maintained cardiovascular variables within narrow physiological limits, so that the arterial pressure did not increase significantly in response to tracheal intubation or during the application of the three-pin headrest. Body temperature was allowed to decrease passively; her nasopharyngeal temperature reached 34°C before cardiopulmonary bypass (CPB).

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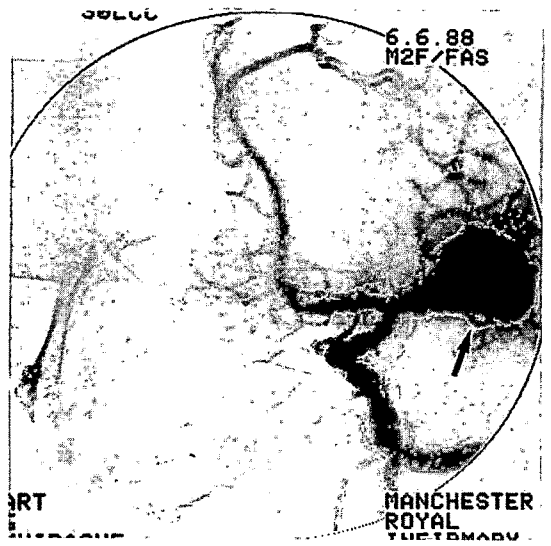

Fig. 1. X ray appearance of the aneurysm before surgery.

The sternum was split during the initial stages of the operation and the heart cannulated and vented before CPB. Thiopentone 40 mg/kg was also given in the 30 minutes before CPB as an aid to cerebral protection. Heparin was then given to maintain an activated clotting time of between 450 and 500 seconds, and CPB established. The patient was cooled rapidly to a nasopharyngeal temperature of 18°. The dura was opened during this cooling period and dissection around the aneurysm started; the mean perfusion pressure was maintained at 40 mmHg. The temperature was reduced to 16°C (the room temperature was 10°C) and the circulation arrested when further dissection was no longer possible. The bulk of the aneurysm sac was then removed and clips applied to complete occlusion of the aneurysm. CPB was re-established after 35 minutes. The patient was rapidly rewarmed to a central temperature of 36.6°C and peripheral temperature of 33°C. Sinus rhythm returned to the heart, which was then decannulated after a total bypass time of 180 minutes. Protamine was given to reverse heparinisation, and the effect was monitored with heparin titration.

The period after CPB was uneventful. Transient increases in systolic arterial pressure to 140 mmHg were treated with boluses of midazolam. Four units of fresh frozen plasma and six units of platelets were given to maintain adequate haemostasis. A subdural pressure monitor was inserted as the dura was closed and at the end of surgery the patient underwent CT scan to exclude the presence of subdural haematoma.

The patient was sedated and ventilated over the first postoperative night and extubated the next morning with no new neurological deficit. Her postoperative course was unremarkable until the 13th day after operation when she developed pleuritic pain. A subsequent ventilation–perfusion scan showed several perfusion defects in both lungs that were consistent with the diagnosis of multiple pulmonary emboli. She was fully anticoagulated and made an uneventful recovery.

Discussion

The use of circulatory arrest in the surgical management of giant cerebral aneurysm is a well recognised technique and was first used in the 1960s. In 1981 Silverburg[2] reported its successful use in a series of eight patients, and in 1988 Spetzler described a series of seven patients with basilar artery repairs, six of whom survived.[3]

Cerebral protection was provided in these cases as in our case by the use of barbiturate coma and profound hypothermia. Barbiturates selectively suppress those cellular mechanisms responsible for the electrical activity of neurones and reduce the cerebral metabolic requirement for oxygen ($CMRO_2$) by as much as 50%.[4] Animal studies have shown a cerebral protective effect of thiopentone when given before an occlusive lesion of the middle cerebral artery.[5] Nussmier was able to demonstrate that thiopentone, given to cause EEG burst suppression, reduced the number and degree of neurological deficits after hypothermic CPB (22°C) when the left ventricle was opened as part of the procedure.[6] The dose required to do this in his series was 40 mg/kg while in Spetzler's series it was 21 mg/kg. Unfortunately, we were unable to monitor the intraoperative EEG and hence chose to give the larger dose.

Hypothermia decreases the cellular metabolism of both neural and glial cells so that the $CMRO_2$ is reduced to a greater extent when barbiturates are used in combination with hypothermia than when either technique is used in isolation.[7] Hypothermia also decreases whole body oxygen consumption to 15% of normal at 20°C and 10% of normal at 15°C.[8] Patients have been cooled to as low as 10°C for some complex cardiac procedures[9] although none of the patients described by Spetzler or Silverburg were cooled below 16°C, which was why we chose this for our

Table 1. Plasma concentrations of atracurium and laudanosine during and before cardiopulmonary bypass.

Time	Rate of infusion atracurium ((mg/kg)/hour)	Temperature °C	% block	Atracurium (μg/ml)	Laudanosine (μg/ml)
Prebypass*	0.6	34	96	1.32	0·71
Time on bypass (minutes)					
5	0.6	30.4	93	1.30	0.11
10	0.6	27.4	92	1.28	0.14
20	0.25	21.8	97	1.51	0.12
34	Off	18.2	99	1.72	0.13
76†	Off	15.4	98	1.24	0.12
140‡	0.42	24.8	96	0.92	—

* Steady state after 180 minutes infusion time.
† Minimum temperature during circulatory arrest.
‡ During rewarming.

lower temperature. The maximum duration of circulatory arrest that can safely be used at this temperature is unknown. However, patients in both Spetzler's and Silverburg's series were arrested for 50 minutes without obvious ill effects.

Atracurium was used to provide muscle relaxation because of its cardiovascular stability and reliability and reversibility of block when given by infusion. We are not aware of any previous reports of its use in profound hypothermia with circulatory arrest, but the use of atracurium infusions during hypothermic CPB is well described, as are the reduced infusion rates required to maintain a constant level of block during hypothermia.[10,11] The concentration of atracurium decreased slightly in the first 10 minutes of CPB and then increased gradually over the next 24 minutes, in spite of a greatly reduced, and then stopped, infusion rate. This increase in concentration may well have been as a result of a decreased rate of atracurium breakdown. Laudanosine concentration decreased dramatically at the start of CPB from 0.71 μg/litre to 0.11 μg/litre. This decrease in laudanosine concentration at the start of CPB suggests that its volume of distribution increases while that of atracurium remains relatively constant.

The slow increase in laudanosine concentration during CPB is what would be expected, in view of the slow rate of atracurium breakdown. Buzello[12] described the effects of hypothermic CPB on neuromuscular transmission in the absence of muscle relaxants and found that the electromyographic (EMG) action potential actually increased with hypothermia. We were surprised in view of this to find that the level of block, as measured by EMG using the Datex Relaxograph, was 98% at 16°C. This occurred in spite of the fact that plasma atracurium concentration was below that required to maintain a 96% block before CPB. This may be explained by the decrease in plasma albumin concentration at the start of CPB. This allowed a greater fraction of atracurium to remain unbound and therefore pharmacologically active.

The rapid identification of a space-occupying haematoma on clinical grounds is impossible in the sedated and paralysed patient. Therefore we decided to scan our patient immediately after operation and to monitor her intracranial pressure (ICP) overnight. Spetzler described seven patients, one of whom developed a subdural haematoma in the immediate postoperative period. Silverburg described eight, one of whom developed an increase in ICP because of temporal lobe swelling. Both Silverburg and Spetzler describe a femorofemoral bypass technique, although we chose to cannulate the heart directly. This allowed us to vent the heart, and avoid the possibility of distension of the left ventricle during ventricular fibrillation. This situation would have damaged the myocardium and made it resistant to defibrillation. It also allowed us to provide excellent venous drainage.

The only major and potentially life-threatening complication became apparent on the 13th postoperative day when our patient developed multiple pulmonary emboli. This may well be relatively common after this procedure. Two of the eight patients described by Silverburg developed pulmonary embolism at 1 and 3 months after surgery. Silverburg believed that the emboli could have originated at the site of femoral cannulation, although this obviously would not have been the case in our patient. The benefits of routine anticoagulation of these patients would have to be weighed against the possible risks after aneurysm surgery.

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CASE REPORT

Management of low cardiac output syndrome after cardiac surgery using enoximone

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Summary

This case report describes the use of enoximone, a potent phosphodiesterase F-IV inhibitor with inotropic and vasodilator actions, to treat low output syndrome after cardiac surgery. The reduced cardiac output was unresponsive to a combination of inotropic drugs and intra-aortic balloon counterpulsation was contraindicated. Cardiac output was increased dramatically by enoximone, but systemic vascular resistance and perfusion pressure remained low until the addition of metaraminol.

Key words

Complications; low output syndrome.
Pharmacology; phosphodiesterase inhibitors, enoximone.

Some patients require temporary inotropic support during recovery from cardiopulmonary bypass. A small percentage develop low output syndrome (LOS), defined as a cardiac index less than 2 (litres/minute) sq m, associated with a systolic arterial pressure less than 90 mmHg and evidence of poor tissue perfusion, which carries a poor prognosis.

The management of these patients is difficult and usually involves the use of inotropic agents and vasodilators to manipulate preload, cardiac contractility and afterload; intra-aortic balloon counterpulsation (IABC) may be required also. However, there are situations when IABC may be contraindicated or disadvantageous (aortic regurgitation, tachyarrhythmias, and vascular disease which affects the aortic bifurcation and iliac vessels), and sole reliance must be placed upon pharmacological support.

The recently introduced selective phosphodiesterase inhibitors with cardiotonic properties have acquired a recognised place in the management of cardiac failure.[1,2] This report describes the use of enoximone (Perfan Injection, Merrell Dow Pharmaceuticals), together with metaraminol, a vasoconstrictor, in a patient who developed refractory cardiac failure after surgery for aortocoronary artery bypass grafting and mitral valve replacement, and in whom IABC was contraindicated.

Case history

A 69-year-old man who weighed 78 kg was admitted from the waiting list with a 2-month history of increasing dyspnoea and angina on exertion, orthopnoea and ankle oedema. He had suffered from scarlet fever as a child and essential hypertension for 15 years, and had been in atrial fibrillation for 2 years. Current medication included digoxin 0.25 mg twice daily, frusemide 40 mg daily, Slow-K two tablets daily, nifedipine 20 mg twice daily, isosorbide mononitrate 20 mg twice daily and warfarin.

He was in controlled atrial fibrillation (ventricular rate 80 beats/minute), with congestive cardiac failure. A chest X ray showed gross cardiomegaly with large left ventricle and atrium, and evidence of early pulmonary oedema. Angiography revealed severe mitral regurgitation, aortic regurgitation, severe quadruple coronary artery disease and a dilated, poorly contracting left ventricle.

He was premedicated with papaveretum 20 mg and scopolamine 0.4 mg one hour before operation. Anaesthesia was achieved with midazolam 3 mg and a gaseous induction with trichloroethylene in 50% oxygen/nitrous oxide; alfentanil 0.5 mg and alcuronium 30 mg were administered after loss of the eyelash reflex. Anaesthesia was maintained with trichloroethylene 0.5%, and papaveretum 20 mg was administered before sternotomy.

Anaesthesia and surgery for mitral valve replacement and quadruple aortocoronary artery grafting were uneventful, and cardiac index was maintained between 1.8 and 2.2 (litres/minute) sq m during cardiopulmonary bypass with a perfusion pressure of 45–60 mmHg. Total bypass time was 152 minutes, with a cold ischaemic time of 99 minutes at a core temperature of 30°C; myocardial

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Table 1. Haemodynamic parameters.

Time (hours after bypass)	Drugs (μg/kg)/minute	Blood pressure (mmHg)	Heart rate (beats/minute)	Left atrial pressure (mmHg)	Cardiac index (litres/minute) sq m	Systemic vascular resistance (dynes second)/cm^5	Urine (ml/hour)
2	Dobutamine 5.0 Adrenaline 2.5	50/30	140	25	1.2	704	<5
4	Dobutamine 5.0 Adrenaline 2.5 Enoximone 10.0	90/50	130	20	—	—	10
20	Dobutamine 7.5 Adrenaline 2.5 Enoximone 5.0 Dopamine 4.0	80/40	130	9	—	—	20
22	Dobutamine 7.5 Adrenaline 2.5 Enoximone 4.5 Dopamine 4.0	85/45	130	10	5.0	424	<5
28	Dobutamine 7.5 Adrenaline 2.5 Enoximone 3.5 Metaraminol 0.15	85/45	125	14	4.4	296	<5
34	Dobutamine 7.5 Enoximone 3.5 Metaraminol 0.04	100/70	148	15	3.0	800	150
44	Dobutamine 7.5	110/70	150	15	3.2	896	150

preservation was achieved using cold potassium cardioplegia fluid and local cooling. Mean systolic pressure after bypass was 50 mmHg, left atrial pressure 6 mmHg and right atrial pressure 2 mmHg. Dopamine was started at a rate of 7 (μg/kg)/minute and small intermittent doses of adrenaline were injected directly into the right atrium until the pressure improved sufficiently to allow decannulation of the heart and reversal of anticoagulation.

There was little improvement after 2 hours; despite infusions of dobutamine and adrenaline (which resulted in a tachyarrhythmia), the systolic arterial pressure was 50 mmHg, heart rate 140 beats/minute, left atrial pressure (LAP) 25 mmHg, cardiac index 1.2 (litres/min)/m^2 and systemic vascular resistance (SVR) 704 (dynes second)/cm^5. Normally he would have been treated by IABC, but this was not feasible because of his tachyarrhythmia and aortic regurgitation. Enoximone was given as an initial slow intravenous bolus of 1 mg/kg, followed by an infusion at a rate of 10 μg/kg/minute. The patient's condition improved sufficiently during the next 90 minutes to allow his transferral from theatre to the intensive care unit where, 4 hours after bypass, his arterial pressure was 90/50 mmHg, heart rate 130 beats/minute, LAP 20 mmHg, and urine output 10 ml/hour.

He remained stable, and 20 hours after bypass his arterial pressure was 80/40 mmHg and heart rate 130 beats/minute, but the LAP had decreased to 9 mmHg and urine output increased to 20 ml/hour; the enoximone infusion was reduced to a rate of (5 μg/kg)/minute.

Heart rate and LAP remained stable over the next 2 hours but urine output decreased to < 5 ml/hour. Cardiac index was 5(litres/minute) sq m, but SVR was only 424 (dynes second)/cm^5. This decreased further to 296 (dynes second)/cm^5 6 hours later, although other haemodynamic variables remained unchanged.

It was decided to give metaraminol in order to increase systemic vascular resistance and to improve perfusion pressure, particularly to the kidneys. Systemic arterial pressure increased to 100/70 mmHg, cardiac index decreased to 3 (litres/minute) sq m, and there were increases in SVR (to 800 dynes second/cm^5) and urine output (150 ml/hour). These changes are summarised in Table 1.

The patient was weaned from the ventilator and made a steady recovery. He was discharged home 2 weeks later, and has since attended the outpatient department on several occasions.

Discussion

Enoximone (MDL 17 043), a selective fraction IV phosphodiesterase inhibitor available for both intravenous and oral use, exhibits direct positive inotropic activity.[3] It also has direct vascular smooth muscle relaxant effects in both animals and man, and improves the efficiency of the failing heart.[4] Installé *et al.*[5] noted increased stroke index (+37%) and cardiac index (+39%) in severe congestive cardiac failure, together with reductions in both ventricular filling pressures (pulmonary capillary wedge pressure −37% and right atrial pressure −35%); these observations suggest improved ventricular compliance.[6] The combination of increased ventricular contractility and compliance, with reduced left ventricular impedance, contributes to the improvement in left ventricular function.

The combination of inotropic and vasodilator therapy often provides greater benefit than either alone, but at the expense of increased rate-pressure product and myocardial oxygen consumption. However, enoximone appears to improve left ventricular function with little change in mean arterial pressure (−9%) or heart rate. The latter increases minimally (+6%) compared to dobutamine (+14%);[5] consequently, there is little effect on rate-pressure product (−2%; dobutamine +17%).[7]

Enoximone possesses bronchodilator properties, and acts also as a pulmonary vasodilator. Consequently, there is a slight reduction in arterial oxygen saturation after its administration, as a result of ventilation/perfusion mismatch secondary to inhibition of hypoxic pulmonary

vasoconstriction. However, the reduced saturation is offset by a marked improvement in oxygen availability.

One of the major objectives when weaning patients from cardiopulmonary bypass is to maintain the diastolic arterial pressure, thus ensuring adequate organ, and particularly coronary, perfusion pressure. The use of potent inotropic agents may increase diastolic pressure at the expense of increased afterload, stroke work and hence myocardial oxygen consumption. The addition of vasodilators to this regimen reduces afterload, allowing an increased inotropic effect without a detrimental increase in SVR; this may not be feasible if mean arterial pressure (MAP) is less than 60 mmHg, because organ perfusion becomes inadequate.

Unfortunately, prolonged use of catecholamines frequently leads to a loss of responsiveness for two reasons. Firstly, the number of β-adrenergic receptors decreases secondary to continued exposure to high concentrations of endogenous catecholamines in chronic cardiac failure.[8,9] Secondly, prolonged elevation of cyclic AMP, due to continued β-receptor stimulation, leads to increases in phosphodiesterase activity and enhances tolerance to β-agonists.[10] High doses of catecholamines may also initiate tachycardia or arrhythmias[11] which worsen myocardial function. These may pose serious problems in patients with low output syndrome, particularly if IABC is ineffective or contraindicated.

Between 3 and 5% of patients require IABC therapy after cardiopulmonary bypass despite recent advances in myocardial protection and inotropic therapy.[12,13] The mortality from cardiogenic shock remains more than 50% despite IABC.[14] These figures correlate well with our experience at Papworth (4% incidence of LOS requiring IABC, with a mortality rate of 46% within 30 days of surgery).

Enoximone is the latest 'noncatecholamine, nonglycoside' inotropic agent which exerts its effects by competitive inhibition of phosphodiesterase F-IV, the isoenzyme responsible for the degradation of cyclic AMP. This leads to accumulation of cyclic AMP, so activating cyclic AMP-dependent protein kinases which catalyse the influx of calcium via slow calcium channels to the contractile elements within the myofibrils.

The normal myocardium is only partially activated during each systole. Contractility is dependent upon the amount of ionised calcium available to contractile elements. Animal experiments have shown that the failing heart, like the healthy myocardium, retains a degree of functional reserve which can be recruited by increasing the amount of calcium available to the contractile system.

This patient showed a dramatic increase in cardiac index from 1.2 to 5 (litres/minute) sq m (+316%) and a reduction in LAP from 25 to 9 mmHg (−64%) after enoximone. SVR decreased from 704 to 424 (dynes·second)/cm^5 (−38%), and over the ensuing 26 hours to 296 (dynes·second)/cm^5 (−57%). Heart rate was affected little; it decreased from 140 to 130 beats/minute (−7.6%). However, metaraminol, a potent vasoconstrictor with predominant α_1-activity (but also some β_1-agonist effects), was required to increase SVR in order to maintain urine output.

Our initial bolus dose of enoximone (1 mg/kg) was at the manufacturer's recommended upper limit (0.5–1 mg/kg up to a maximum of 3 mg/kg).[15] Rigauld *et al.* used doses of 1.5–2 mg/kg,[16] although Bristow[17] stated that arrhythmias became a problem at doses over 2 mg/kg. In the light of more recent work[18] it may be more prudent to scale down the initial dose to 0.5 mg/kg which can then be repeated if the result is ineffective.

The manufacturer's data sheet[15] suggests that enoximone may be administered either by intermittent injection or by continuous infusion, but controversy exists over the best method of maintenance treatment. Recently, Gonzalez *et al.*[1] used an initial dose of 1 mg/kg and recommended a continuous infusion of 10 μg/kg/minute starting 2 hours later. However, Vincent *et al.*[18] restricted the initial dose to 0.5 mg/kg and believed that a continuous infusion was not indicated in view of its prolonged effect. The drug is metabolised by hepatic oxidation to an active metabolite, 75% of which is excreted unchanged in urine, and has a long duration of action after a single intravenous bolus (1.5–4 hours). This is probably due to the duration of intracellular effect rather than the plasma half-life of the parent drug or its metabolite.

Crawford[19] noted adverse effects in 20% of a series of 119 patients from five centres treated with enoximone (up to 3 mg/kg) for severe congestive heart failure; arrhythmias, nausea and vomiting and insomnia were the most common. The most serious adverse effects were ventricular tachycardia (3.4%) and hypotension (2.5%).

Enoximone was effective in improving cardiac function in this patient with severe, refractory low output syndrome after cardiac surgery. It may offer a particular advantage to patients in whom conventional inotropic agents are ineffective because of tachyphylaxis, or in situations in which the dose is limited by tachycardia or severe arrhythmias, or intra-aortic balloon counterpulsation is either unavailable or contraindicated. However, it can also be a potent vasodilator and the reductions in SVR and MAP may necessitate the administration of a vasoconstrictor agent to maintain organ perfusion. It may be prudent to use an initial dose of 0.5 mg/kg, which can be repeated if necessary.

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SPECIAL ARTICLE

Peri-operative care in restrictive respiratory disease

J. A. PATRICK, M. MEYER-WITTING, F. REYNOLDS AND G. T. SPENCER

Summary

A total of 139 of 473 severely disabled, mainly ventilator-dependent patients required some form of surgery. Such patients require surgery more frequently than normal individuals, both because of their disability and because even minor unrelated disorders superimposed on permanent disability cause greater handicap. We report the peri-operative management and postoperative complications of 142 operations on 83 patients between 1982 and 1987. A simple inhalational anaesthetic technique was used; opioids and muscle relaxants were seldom given. Negative pressure ventilation was employed in the postoperative period when appropriate, and was combined with vigorous chest physiotherapy. There were three peri-operative deaths, but the overall death rate in the patients who underwent surgery was no greater throughout the study period than in those who did not require surgery. We believe that an aggressive surgical approach is appropriate in severely disabled, ventilator-dependent patients.

Key words

Lung; restrictive lung disease.
Ventilation; mechanical, negative pressure.

The St Thomas' Hospital Respiratory Unit cares for severely disabled patients many of whom require long-term mechanical ventilatory support. The unit has 16 inpatient beds and provides a domiciliary equipment maintenance service manned by four technicians who travel 200 000 miles annually. This enables even those patients who require continuous mechanical ventilation to live at home,[1–3] while all have direct access to the Unit when necessary. The patients come from all regions in the United Kingdom and elsewhere. They are admitted for initial assessment; when acutely ill; for rehabilitation; by tertiary referral for tracheostomy closure and weaning from positive pressure ventilation; or for surgery.

These patients may require surgery as a direct result of their disabilities, because of very minor disorders which, in the presence of severe disability, may greatly reduce functional capacity, or for the same reasons as other people (e.g. appendicectomy, prostatectomy).

Anaesthesia and surgery for such patients are often considered to be risky. Postoperative complications have been reported[4,5] and many patients admitted to the Respiratory Unit had been refused surgery elsewhere. The most commonly cited reports of anaesthesia for patients with severe pulmonary diseases have been concerned largely with severe chronic obstructive airways disease (COAD)[6,7] and the respiratory cripples of Utting *et al.*[8] were elderly patients with emphysema or COAD. The patients reported here do not fall into this category. We have examined their records and reviewed their need for surgery, the peri-operative management and the outcome.

Patients

A total of 559 patients were referred to the Unit up to the end of 1987. The notes of 86 who died before 1982 were unavailable or incomplete, and thus it was necessary to confine the study to the six years between 1982 and 1987 in order to compare the mortality between the surgical and nonsurgical groups. One hundred and thirty-nine of the remaining 473 patients (29.4%) had undergone one or more operations. Thirty-six individuals who were still patients of the Unit during this time had operations before 1982; they were excluded, as were a further 20 physically disabled patients who had surgery but no respiratory disability.

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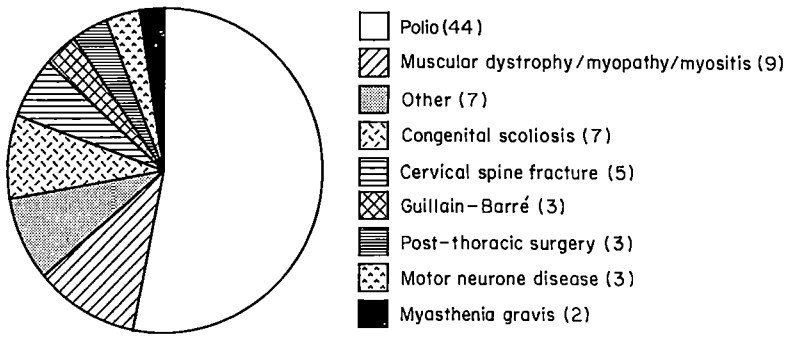

Fig. 1. Diagnosis of patients in the study group.

The remaining 83 patients, aged 22–76, are the subject of this report. Their original diagnoses are shown in Figure 1. A total of 142 surgical procedures were carried out under general anaesthesia during the study period.

The study group has been classified according to respiratory dependence (Table 1) rather than by vital capacity, since there is considerable overlap between measured vital capacity and the degree of respiratory assistance used regularly. Forced vital capacity is given in this paper as an absolute value and not as a percentage of predicted. Normal values cannot be predicted accurately in severe disability because of limb and trunk deformities and body weight discrepancy.

Type of operation

The types of operation are shown in Figure 2. Most orthopaedic operations were related directly to the disability, e.g. scoliosis surgery ($n = 4$), fractures resulting from trauma and decalcification after muscle weakness ($n = 4$), degenerative joint disease that required joint replacement ($n = 4$), and carpal tunnel decompression in manual wheelchair or crutch users ($n = 2$). Urological procedures were related usually to urolithiasis after demineralisation resulting from immobility. Stone formation is further favoured by respiratory acidosis which elevates nonprotein-bound serum calcium.[15,16]

Gynaecological operations included minilaparotomy which was required rather than laparoscopy for sterilisation in two deformed scoliotic women. Hysterectomy was necessary in four severely disabled women who had difficulty in managing menstruation. Four women with scoliosis developed cardiorespiratory failure which necessitated respiratory support during pregnancy,[17] and required Caesarean section for medical or obstetric reasons, e.g. contracted pelvis.

The patients underwent a variety of otorhinolaryngological procedures. Fifteen had surgical closure of tracheostomy and will be the subject of a separate report. Laryngotracheobronchoscopy was a common procedure

Table 1. Respiratory dependence in the study group.

Grade (number of patients)	Mean adult vital capacity ml (range)	Spontaneous ventilation	Mechanical aid (number of patients) References 2, 9–13		
0 (7)	1405 (1000–1830)	Always	Nil. Tracheostomy only, e.g. bulbar weakness		
I (25)	1160 (400–2400)	Always unless ill	Noninvasive, e.g. iron lung		
			Day	*Night*	
II (23)	1067 (augmented by GPB*) (600–1800)	Only while awake using accessory muscles	Nil Coughing aids†	Cuirass Tunnicliffe jacket Rocking bed (if paralysed diaphragm)	(7) (8) (9)
III (14)	620 (augmented by GPB*) (300–1050)	Part of day only	As night aid prn Coughing aids†	Iron lung Positive pressure mouthpiece IPPV‡	(6) (3) (4)
IV (14)	60 (0–350)	Nil	IPPV‡ Iron lung§	(11) (3)	

*GPB, glossopharyngeal breathing ('frog breathing')[14] where serial incremental inflation of the lungs is produced by gulping air into the oropharynx, closing the mouth and soft palate, opening the larynx and forcing the air from the pharynx into the trachea, enabling the patient to take a breath 3–4 times the normal vital capacity.

†Commonly, mouthpiece and pressure-triggered ventilator.

‡Usually the East Radcliffe, a time-cycled pressure generator, via tracheostomy.

§One patient uses a pneumobelt[9] during the day. One patient survives on continuous GPB* and uses the iron lung at night.

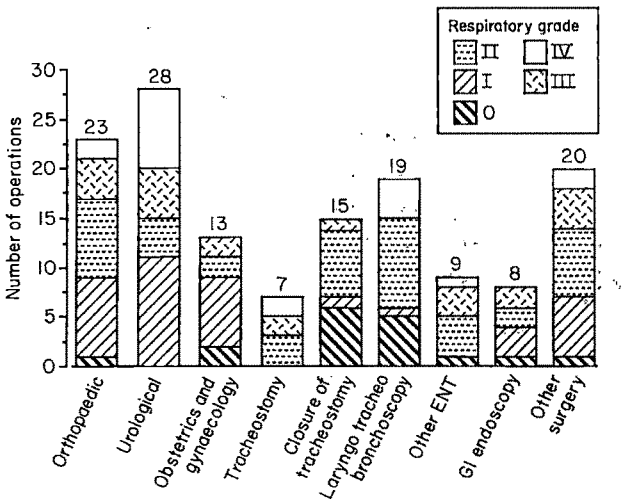

Fig. 2. Type of operation and respiratory grade.

($n = 19$) for airway assessment. Surgery was required also for postnasal drip or nasal airway problems which, although clinically insignificant in normal individuals, were the cause of considerable morbidity in these patients. Eight patients underwent gastrointestinal endoscopy under general anaesthesia to allow control of the airway and ventilation; patients who are dependent on their voluntary muscles for ventilation would be at considerable risk during conventional sedation for endoscopy.

A wide range of other surgical procedures that ranged from lumpectomy to open heart surgery, but excluded varicose vein surgery and hernia repair, was performed. Two patients had small chest wall lesions removed because they were interfering with cuirass ventilation.

Peri-operative management

Preparation

All patients were visited pre-operatively by a physiotherapist who explained and demonstrated the postoperative physiotherapy procedures. Patients who were thought likely to require postoperative negative pressure ventilation in an iron lung and who were unfamiliar with it were trained before operation. Insertion of a nasogastric tube was avoided if possible when postoperative negative pressure ventilation was planned because of the risk of gastric distension.

Premedication

Atropine 0.6 mg was given intramuscularly. Sedative premedication was avoided. Prophylactic anticoagulants were not given and antibiotics were used only when surgically indicated.

Anaesthesia

All patients were anaesthetised by one of the authors (G.T.S.). Induction of anaesthesia was achieved using thiopentone; anaesthesia was maintained according to the algorithm in Figure 3, except for bronchoscopy when oxygen via venturi and intravenous thiopentone were used. Some patients had a pre-existing tracheostomy, but in the remainder tracheostomy was performed only if there was a primary indication, e.g. bulbar weakness; *no* patient underwent tracheostomy as part of the peri-operative management of another procedure. It was impossible to intubate the trachea in two patients without tracheostomy, but these patients had several operations in which artificial ventilation was applied via a face mask.

Anaesthesia was maintained using nitrous oxide in oxygen with low concentrations of volatile agents. Intraoperative opioids were used rarely, and then sparingly. Nondepolarising muscle relaxants were rarely necessary. Ventilation was usually assisted by hand, but occasionally a Manley Pulmovent was used. Blood was replaced if losses exceeded 200 ml.

Illustrative case 1. A solicitor with grade IV respiratory dependence who had poliomyelitis at the age of 34 had virtually no vital capacity. However, he had refused a tracheostomy and positive pressure ventilation (IPPV) because he liked to wear a tie. He normally used an iron lung at night, but during the day he survived with a pneumobelt[9] and continuous glossopharyngeal breathing,[14] at which he was adept.

He required a total hip replacement at the age of 57, but it was impossible to intubate his trachea after induction of anaesthesia because of a rigid neck and jaw. The operation proceeded under mask anaesthesia with assisted ventilation by hand. There was heavy blood loss and eight units of blood were transfused. Postoperatively, he was nursed in a rotating iron lung[10] until wound healing permitted use of his pneumobelt. The only complication was a minor wound infection. He underwent cystoscopy with removal of bladder stones 6 months later and transurethral resection of prostate one year later, both with the same anaesthetic technique. He recovered uneventfully on both occasions.

Postoperative management

Respiratory support

The immediate management in the recovery room was determined by the degree of respiratory dependence, the type and duration of operation, the blood loss and the wound site. The aim was to return patients to their previous level of respiratory support as quickly as possible (Fig. 3). Patients with grade IV respiratory dependence who required continuous IPPV returned immediately to this form of support using their home ventilator. Those with relatively mild respiratory dependence (grade 0–I) usually recovered without respiratory aids. Patients of intermediate grades (II–III) who had undergone minor surgery generally required support with their own respiratory aid or in an iron lung until they were fully awake and able to breathe adequately unaided. Those with grade II or III disability who had prolonged surgery or procedures with heavy blood loss required some form of ventilatory support at least until they were awake, warm and their cardiovascular systems stable, and often for a few days afterwards; the rotating iron lung[10] was used frequently in this group.

Illustrative case 2. A 52-year-old woman who had poliomyelitis at the age of 14 had a vital capacity of 800 ml and normally used a positive pressure mouthpiece at night (grade II respiratory dependence). She required fixation of

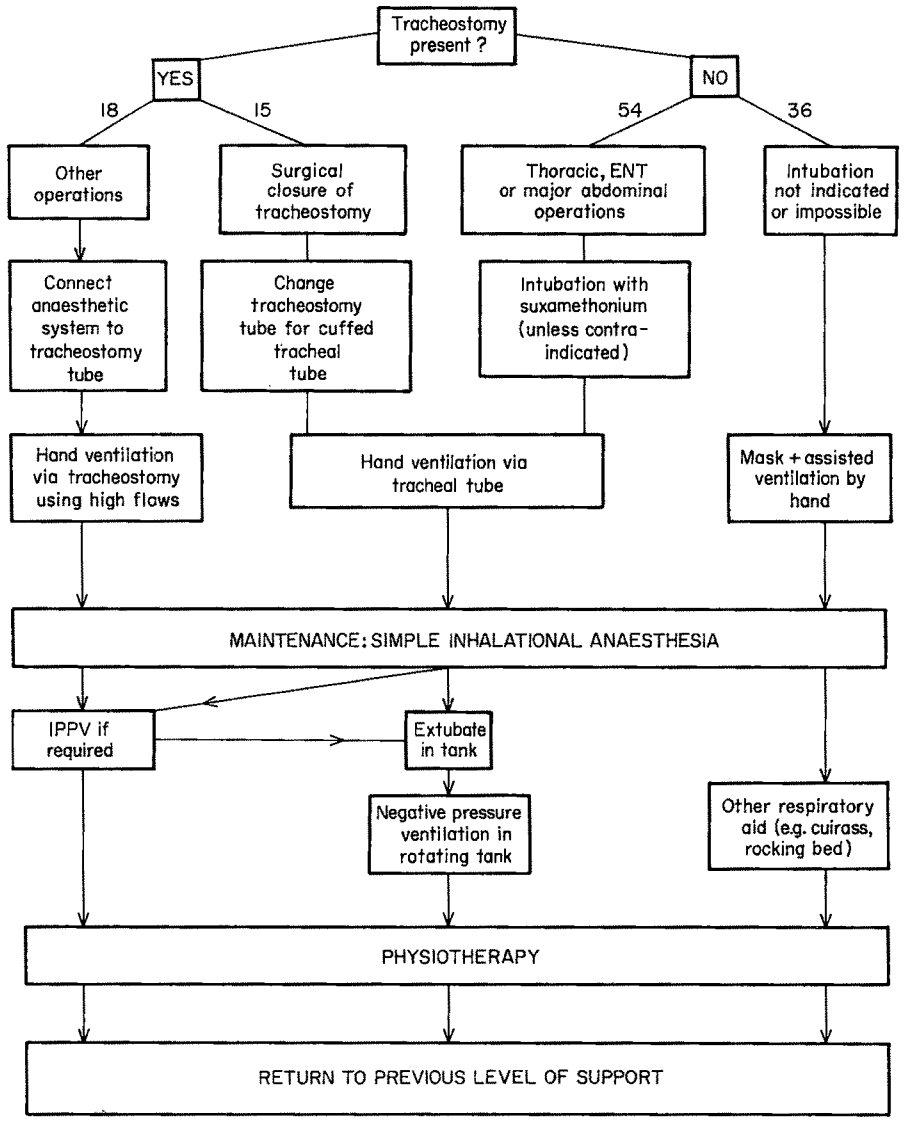

Fig. 3. Peri-operative management.

a fractured femur after a road traffic accident. However, she was unable to use her mouthpiece because she had suffered facial trauma in the accident. She was managed successfully in an iron lung after surgery until her facial lacerations had healed. She underwent two cystoscopies and dilatation and curettage on other occasions, and used her mouthpiece as normal after each of these procedures.

Illustrative case 3. A 24-year-old man with nemaline myopathy had a vital capacity of 800 ml. He normally used a Tunnicliffe jacket[9,18] at night for grade II respiratory dependence. A fractured humerus prevented the use of this device and he was nursed in an iron lung after internal fixation of the humerus until the wound had healed.

IPPV via tracheal tube was required only if the type of surgery made iron lung ventilation unsuitable in the post-operative period, e.g. after spinal fusion, but the trachea was always extubated in the iron lung as part of the weaning process (Fig. 3).[19]

Analgesia

Postoperative analgesia was provided usually by relatively low doses of intramuscular papaveretum.

Physiotherapy

All patients were visited regularly by the physiotherapist in the postoperative period and received treatment in the rotating iron lung when appropriate.

Postoperative complications

The postoperative complications in the study group are shown in Table 2. Pulmonary complications were the most

Table 2. Postoperative complications.

	Number
Chest infection	10
Other infections	5
Respiratory insufficiency	7
Ileus	3
Other	9
Pulmonary thromboembolism	0
Death	3

frequent. There were 10 (7%) bacteriologically and/or radiologically documented episodes of pulmonary infection. They were treated with physiotherapy, antibiotics and negative pressure ventilation. One of these patients had grade I respiratory dependence, four grade II, four grade III and one grade IV.

Seven patients developed postoperative respiratory insufficiency which was noninfective in origin. Three had grade 0 respiratory dependence, two grade II, one grade III and one grade IV. These included two patients who developed acute respiratory failure after opioid analgesia (one after intramuscular papaveretum 10 mg, the other after intravenous diamorphine 2.5 mg) and who required tracheal intubation and IPPV. Three developed problems after formal closure of tracheostomy; in two, it was necessary to re-open the tracheostomy and in the other the trachea was intubated; this patient continued to require nocturnal ventilation in an iron lung after extubation. Another patient aspirated stomach contents despite the presence of a cuffed tracheostomy tube. The seventh of this group required emergency tracheostomy because of profuse bleeding after laser surgery of a tracheal stenosis secondary to a previous tracheostomy during acute poliomyelitis in 1955.

Two patients developed weaning problems after the use of large doses of sedative drugs during postoperative IPPV in another unit, but in each case the trachea was extubated successfully in the iron lung when the depressant effects of the drugs had worn off.

Deaths

Three patients died during the first 30 postoperative days (the CEPOD limit for postoperative mortality).[20]

Illustrative case 4. A 23-year-old male was tetraplegic and IPPV-dependent (grade IV) after fractures of his third and fourth cervical vertebrae sustained in a road traffic accident 15 months previously. After laparotomy for division of adhesions, he developed pneumonia which was not treated actively in view of his general condition and outlook, and he died 7 days later.

Illustrative case 5. A 56-year-old man with a vital capacity of 1500 ml and grade II respiratory dependence after poliomyelitis 34 years previously, developed an acute confusional state and a hemiplegia 2 days after an emergency ureterolithotomy. He remained confused for the next 2 days, and developed an ileus and renal failure. He had a cardiac arrest, from which he could not be resuscitated, on the eighth postoperative day. At autopsy, he was found to have suffered an internal capsule haemorrhage.

Illustrative case 6. A 32-year-old man with poliomyelitis since infancy, scoliosis, a vital capacity of 1500 ml, grade I respiratory dependence and who abused drugs, required incision and drainage of a thigh abscess. He recovered from this uneventfully, but died at home from a self-administered drug overdose 2 weeks later.

The peri-operative mortality was 3.6%. Another 18 patients in the study group died between 6 weeks and 2 years after operation (outside the peri-operative period),[20] usually as the result of progressive conditions such as motor neurone disease ($n = 3$) or carcinomatosis ($n = 5$). The total mortality in the study group was 25.3% and 20.4% in the entire surgical group (103 patients) compared with 18.3% in the group who had no surgery. There is no significant difference in the mortality between the surgical and nonsurgical groups.

Discussion

Several aspects of management contributed to successful peri-operative outcome. Sedative premedication must be avoided in patients who require to stay awake to breathe unaided (Table 1) because of the risk of respiratory depression.

Intra-operative care

Elective pre-operative tracheostomy was avoided deliberately. It is unnecessary if efficient noninvasive postoperative respiratory support is provided. A tracheostomy in patients with permanent respiratory muscle weakness usually requires formal surgical closure, and even minimal stomal site stenosis may cause permanent worsening of respiratory status.

Patients with a pre-existing tracheostomy and a noncuffed tube received manual ventilation of the lungs during surgery, via their normal tube. A cuffed tracheostomy tube was used only during oesophageal or nasal surgery where substantial bleeding into the upper air passages was anticipated, or in the presence of acute intestinal obstruction. A cuffed tube may be difficult to insert without dilatation of the stomal site and can cause persistent stomal leaks when removed. Laryngeal air leaks during unconsciousness can be controlled by throat pack, though this has rarely proved necessary.

IPPV may cause profound changes in arterial P_{CO_2} in this group of patients who, despite decreased muscle mass and low carbon dioxide production, are often accustomed to a high arterial P_{CO_2} secondary to hypoventilation, with loss of sensitivity to carbon dioxide. End-tidal CO_2 monitoring might be useful to prevent gross hypocapnia during controlled ventilation, but was not available for most of the patients described here. Direct blood gas monitoring was avoided when possible because of the hazards of indwelling cannulae in patients with paralysing diseases. We have found that peripheral arteries are of very small diameter in the presence of severe wasting, and that the risks of cannulation are increased. Ventilation by hand was used when appropriate to assist the patient's spontaneous respiratory efforts, to avoid difficulties in re-establishing spontaneous ventilation after IPPV.

Many of the patients have virtually no abdominal muscle mass and marked respiratory muscle weakness; consequently, muscle relaxants are rarely required. Any discussion of sensitivity to non-depolarising neuromuscular blocking drugs in the various neurological conditions is therefore largely academic. Opioids were avoided during operation in order to minimise the risk of postoperative respiratory depression.

Many of the patients in this series had low blood volumes secondary to reduced muscle mass, and careful restoration of circulatory volume was essential during surgery. Blood transfusion is indicated in these patients earlier than in able-bodied individuals.

Regional anaesthesia was found to be inappropriate. Anatomical abnormalities may make it technically difficult and unpleasant for the patient. Surgery may require a disabled, deformed patient to be placed in a position on the operating table, such as lithotomy, which is as painful as

the procedure. The operative position may further impair the patient's spontaneous ventilatory capacity, particularly if the diaphragm is paralysed. Unconsciousness and assisted ventilation are preferable.

Postoperative management

Every patient was considered to be at risk from postoperative pulmonary complications, and although the reported frequency was not great, all received prophylactic treatment. Most patients could return immediately to their usual form of respiratory assistance, but modification was sometimes necessary because of the type of operation. For example, patients who were normally cuirass-dependent at night, but who had abdominal wounds, were ventilated in an iron lung postoperatively because cuirass ventilation would have been painful. (See also cases 2 and 3).

The iron lung is particularly useful in this group of patients because it provides noninvasive ventilatory support without the need for sedation and allows the patient to eat and sleep. Consequently, it permits extubation in the absence of adequate spontaneous ventilation and avoids prolonged IPPV with its attendant problems. Supplementary oxygen can be given via nasal cannulae if required. The Kelleher rotating iron lung, in which the cabinet can be completely inverted,[11] allows the patient to be positioned prone or semiprone for sputum clearance while negative ventilation is continued; it is therefore an invaluable aid to physiotherapy.

Three maternal deaths have been reported in scoliotic women,[5] in whom negative pressure ventilation might have been life-saving. We have experience of pregnancy in 19 scoliotic women, five of whom have been reported elsewhere.[17] Eight required ventilatory support, seven for the first time in pregnancy. Seven have continued to need some form of ventilatory support since.

Effective expulsion of secretions by coughing normally requires an intake of breath of at least 1.5 litres.[21] Patients with long-standing muscle weakness and a forced vital capacity below this value develop compensatory manoeuvres to permit coughing (such as abdominal compression or glossopharyngeal breathing) or use mouthpiece coughing aids (Table 1). Such manoeuvres are difficult in the postoperative period, when forced vital capacity may be reduced by anaesthesia and wound pain. Aggressive physiotherapy is therefore essential to minimise pulmonary complications. Wound pain is reduced in the presence of muscle weakness and it is appropriate to minimise opioid administration in order to avoid respiratory depression.

Subcutaneous heparin does not appear to be indicated. We have no record of deep vein thrombosis in patients with flail limbs or severe muscle wasting despite their immobility. Pulmonary thromboembolism did not occur in the study group; the only case in this unit occurred in 1981 when a 48-year-old woman (grade II) with a vital capacity of 500 ml died suddenly 10 days after appendicectomy. At autopsy, a massive pulmonary embolus was found. However, she had 'upside down' poliomyelitis that affected mostly her trunk and arms, and did not have wasted legs.

Conclusion

Minor additional disorders superimposed on a permanent disability cause greater hardship and handicap than a similar disorder in an otherwise able-bodied person. Prompt surgical treatment of intercurrent surgical conditions is therefore particularly important in this group of patients. Many of the patients in this report were denied surgery at other institutions on the assumption that perioperative risk from their pre-existing disability would be too high. Our experience does not support this view but suggests that their surgical needs should be assessed on surgical grounds alone. The use of simple anaesthetic techniques, minimal dosage of muscle relaxants and narcotics, combined with vigorous postoperative chest physiotherapy using the Kelleher rotating iron lung and early mobilisation, have permitted normal or even aggressive surgical practice to be employed successfully.

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Forum

Iatrogenic anaemia?

A survey of venesection in patients in the Intensive Therapy Unit

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Summary

In 30 consecutive patients admitted to the Intensive Therapy Unit, the volume of blood taken for investigations was recorded. Results were available for 26 patients. Total venesection volume averaged 336 ml. Venesection volume averaged 55.7 ml/day after the first 24 hours. The mean haemoglobin on admission was 11.5 g/dlitre. Blood loss was related to both APACHE score and length of stay (APACHE.day), to the presence of arterial and central venous catheters, and to the need for mechanical ventilation. Iatrogenic blood loss of this magnitude will cause anaemia if it continues.

Key words

Intensive care.
Measurement; blood loss.

Anaemia is said to be a common problem in patients who receive intensive therapy. This statement is unproven, but generally accepted. The anaemia is seldom severe because most clinicians acknowledge the need to maintain oxygen delivery and transfuse patients whenever the haemoglobin value decreases below 10 g/dlitre.

The well recognised causes of anaemia include haemolysis (and disseminated intravascular coagulation), haemodilution, inadequate nutrition and that due to drugs, or other toxins (for example, aluminium). It is probable that many of these causes (particularly nutritional anaemias) play only a small part in production of most anaemias, at least for the majority of patients admitted to the Intensive Therapy Unit (ITU). Bone marrow failure (as opposed to aplasia), shown by a relatively reduced peripheral reticulocyte count, may occur and would compound any other cause. The reason for bone marrow failure is probably multifactorial. The most likely cause for anaemia is concealed or revealed blood loss due to, for instance, gastric erosions or the insertion of large-bore central lines, such as pulmonary arterial catheters. Obviously, recent surgery may be implicated.

Some potential causes of anaemia are amenable to prophylaxis (for example, H_2 receptor antagonists to prevent stress ulcers in the stomach), but other causes are effectively uncontrollable, or unresponsive to therapy: large doses of haematinics appear to have little effect upon the reticulocyte count or marrow response, and many drugs cannot be omitted.

One feature of intensive therapy, amenable to change, is the requirement for multiple blood samples for repetitive arterial blood gas analysis, for regular electrolyte measurement or for multiple blood cultures. We were unclear about the magnitude of our patients' iatrogenic blood loss, so we measured it in a consecutive group of our patients.

Method

The volumes of all blood samples are entered on ITU charts by the nursing staff as part of our assessment of fluid balance. No additional volume is included for 'deadspace' wastage, if blood has been drawn from indwelling vascular catheters.

A retrospective study was performed on a cohort of 30 patients who were admitted to the ITU. The first patient was chosen at random, and then in order of admission 30 case records were studied.

We noted the daily venesection volume and daily haemoglobin measurement. The volume of blood transfused could be calculated from the ITU charts because all blood bags used are separately weighed, and almost all blood supplied to the ITU is red cell concentrate. The presence of arterial, central venous, pulmonary artery, or dialysis/continuous arteriovenous haemofiltration lines was noted, as was the requirement for mechanical ventilation. The patient's APACHE II score for the first 24 hours and expected APACHE outcome[2] and actual outcome were obtained from the ITU database.

Results

Full information related to venesection was available for 26 of the 30 patients (87%). In the four patients excluded, the only information missing was the volume of blood venesected at admission.

Table 1 gives comparable information about our sample cases and those of our annual intake of patients. Patients in whom arterial lines were present had a higher mean APACHE score than those without (21.8 compared with 12.3 ($p < 0.02$)). There was no difference between this group and all the patients admitted to the ITU during that year (Table 1).

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Table 1. Comparison of sample group and population.

	Sample group (26)	Population (148)
APACHE II score, mean (range; SEM)	18.15 (5–38; 2.09)	19.19 (3–46; 0.87)*
Expected mean risk of death, % (range)	35.2% (0.6–93.4)	37.0% (0.29–98.04)*
Actual death rate, % (*n*)	38.5% (10)	37.8% (56)*
Arterial cannulae, % (*n*)	61.5% (16)	60.8% (90)
Central venous catheters, % (*n*)	73.1% (19)	82.4% (122)
Pulmonary artery catheters, % (*n*)	19.2% (5)	18.9% (28)
Mechanical ventilation, % (*n*)	65.4% (17)	65.5% (97)
Haemodialysis/haemofiltration, % (*n*)	7.7% (2)	10.1% (15)
Average stay, days	5.5	5.86

*$p > 0.5$, NS.

The mean total venesection volume for the patients was 336 ml with an average daily loss of 66.1 ml. However, this ranged from 28 to 108 ml/day. An average of 85.3 ml was drawn on the first day, but this volume ranged from 33 to 127 ml. Total blood loss at 72 hours averaged 164 ml. Arterial blood gas analysis accounted for 130 ml of the cumulative loss of 336 ml. If day 1 is excluded, the mean total venesection volume for all patients was 250.9 ml. The number of patients from which this value was obtained decreased from 26 on day 1 to 14 by day 3. In patients in whom an intra-arterial line was present, average venesection volume was 480 ml compared with 105.8 ml for those patients without ($p < 0.01$). When a central venous catheter was present, the mean venesection volume was 413.8 ml compared with 125.1 ml ($p < 0.02$) in those in whom no central venous line was present.

The mean venesection volume was 562 ml in the group of 12 patients who required both mechanical ventilation and in whom an arterial line was present, but this volume was not different from any patient with an arterial line (480 ml; $p > 0.5$).

The mean haemoglobin concentration of the patients, on admission, was 11.52 g/dlitre. Patients were transfused a mean volume of 818 ml (148 ml/day). This ranged from zero in 14 patients to 4055 ml in one patient. However, when expressed as blood transfused/patient/day this figure was 121 ml/day. The mean volume used was 1934 ml for the 11 patients receiving blood. They received on average 206 ml of blood/day during their average stay of 9.4 days.

Table 2. Routine venesection policies: ITUSCH.

	Investigations	Volume (ml)
On admission	Arterial blood gas, packed cell volume, sodium, potassium, colloid osmotic pressure*	5
	SMAC	5
	Full blood picture, platelets	5
	Coagulation	5
	Blood group*	10
	Hepatitis-associated antigen,* virology	10
	Endocrine (thyroid-stimulating hormone, thyroxine, tri-iodothyronine, cortisol)	10
	Vitamins* (B_{12} and folate)	10
	Serum save (deep frozen)	10
Daily	Arterial blood gas, packed-cell volume, colloid osmotic pressure, sodium, potassium†	5
	Full blood picture, platelets	5
	SMAC	5
	Coagulation	5
Weekly	Synacthen test	15
	Serum save (deep frozen)	10

*May be omitted. SMAC, sequential multi-analyser with computer.
†ITU Stat laboratory.

Discussion

This study shows that considerable quantities of blood are drawn from patients in this ITU. This would go some way to explain our impression that patients who require intensive therapy for long periods have a tendency to become anaemic and require red cell transfusion.

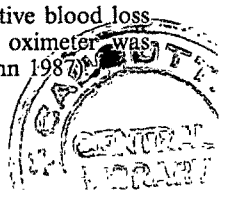
All patients receive a routine battery of investigations (see Table 2) on admission to this ITU. This makes an immediate venesection of 60 ml blood necessary; 5 ml is usually taken for use in the ITU Stat laboratory for measurement of blood gases, haematocrit, sodium and potassium, and oncotic pressure. Routine daily investigations (see Table 2) require a 15-ml venesection; additional investigations are usually possible and are arranged by the laboratory by sample splitting. A variable number of blood gas analyses are performed, but this is seldom less than three (equivalent to 6 ml) if the patient receives controlled ventilation for more than 24 hours. Weekly investigations require a further 25 ml venesection (Table 2).

Blood was always drawn from the patient using a syringe and it was this volume which was recorded. We use vacutainers which draw a measured volume, but we do not use this technique to venesect directly.

The APACHE score of this group of patients does not differ from the mean APACHE score for all the patients admitted to the ITU. Table 1 shows that the study group appeared representative of the whole year in all other parameters, so that it seems reasonable to assume that this study reflected our patient population and thus our venesection practise for all our patients. Venesection policy did not change during an 18-month period, which included the study period.

Our average measured (cumulative) venesection volume, after the first 24 hours was 251 ml, but there were wide fluctuations. Not surprisingly, the presence of either an arterial or central venous line was associated with greater venesection, and it is tempting to speculate that ease of access encourages venesection. However, there is a clear association between 'sickness', (APACHE score), the presence of an arterial line and venesection volume. Total blood loss is related to both length of stay in the ITU and the APACHE score (APACHE.day) (Fig. 1).

A mean volume of 130 ml blood (23.6 ml/day) was used for arterial blood gas analysis. Sixty-five percent of patients required mechanical ventilation and 12 (70%) of these 17 patients had arterial lines: the presence of the latter seems to be associated with both a bigger cumulative blood loss and a higher APACHE score. No pulse oximeter was available during the period of study (Autumn 1987).



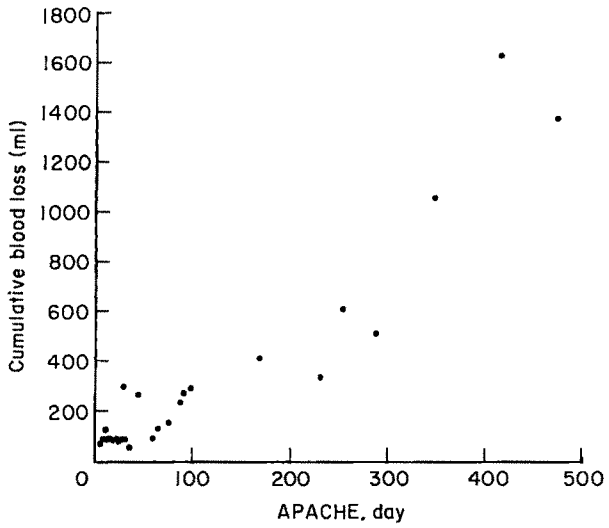


Fig. 1. The relationship between blood loss and APACHE.day.

The single biggest unpredictable volume loss was that due to blood culture. All vascular lines are cultured, so this volume could be large.

Assuming our averages are representative, the cumulative venesection volume, expressed as a weekly volume, is approximately 427 ml. Even if the first 24 hours is excluded (when venesection includes multiple screens such as hepatitis associated antigen), this figure is still 390 ml/week (55.7 ml/day). This may be a more representative figure, but it remains a notable blood loss. A chronic loss of over 20 ml/day produces a negative iron balance in an otherwise well-nourished patient with a normal bone marrow.[3] Our patients' average cumulative loss of 336 ml over 5.5 days represents a loss of about 125 mg elemental iron, assuming an average haemoglobin of 11.5 g/dlitre. The parenteral nutrition additive solution, 'Addamel' (10 ml) contains approximately 13.5 mg iron.

Our patients' blood loss seems large, but in the only other study of this nature, Henry[4] showed a much greater iatrogenic loss in patients who had undergone cardiac surgery, with a mean loss of 377 ml in the first 24 hours. The volume loss for patients admitted to the general surgical intensive care unit, a more comparable group, was 240 ml in the first 24 hours. These figures, unlike ours, include deadspace wastage, so our patient loss seems more modest.

The mean haemoglobin on admission was 11.52 g/dlitre. In this ITU, efforts are made to maintain the haemoglobin in excess of 10 g/dlitre or higher if oxygen delivery is compromised. Our results show that we transfused patients an average of 818 ml blood, but we do not believe this to represent the volume of transfusion needed to avoid iatrogenic anaemia. Review of the records showed that all but two of the transfused patients had active surgical bleeding. The other two patients were transfused early in their stay for nonsurgical anaemia: no patient appeared to be transfused because of iatrogenic (venesection) blood loss.

We conclude that significant quantities of blood are withdrawn from patients for a variety of routine investigations. In short-stay patients this loss should be tolerable. The same may not be true for long-stay patients, who may require red cell transfusion as a direct consequence of iatrogenic losses. We have reviewed both the usefulness of our 'routine' investigations, and the sample volumes supplied to the laboratory since this study. We have reduced some of our supplied volumes, and the replacement of our blood gas machine has reduced the sample volume needed for measurement of arterial blood gases. The effect of continuous pulse oximetry upon our need for repeated arterial blood gas estimation (24 ml/day) will be interesting.

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Intravenous cannulae colour coding

A perennial source of confusion

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Summary

There is no standard colour code for intravenous cannulae in the United Kingdom. A questionnaire was sent to the manufacturers to compile a table of available cannulae, and to assess their views and plans with regard to colour coding. Present moves to establish an international standard are outlined. A simple colour coding standard is proposed.

Key words

Equipment; cannulae, coding.

There is currently no standard colour code for intravenous cannulae in the United Kingdom to which manufacturers must adhere. This has led inevitably to the manufacturers' production of cannulae to their own arbitrary standards. The resulting chaotic situation has important clinical implications, some of which have been highlighted by Stehling.[1] It has been suggested that consensus among manufacturers may be achieved if pressure were brought to bear by concerned clinicians.[2] A survey of cannulae in current use was carried out to clarify the present situation together with a single report of manufacturer's views with regard to the need to conform to a national or international colour standard.

Method

A questionnaire was sent to the nine manufacturers who supply intravenous cannulae to the UK market and requested a list of their cannulae sizes together with the corresponding colour code. In addition these questions were asked: Are you aware of any colour coding standard applicable to intravenous cannulae? Would you be in favour of adopting a standard? Are you aware of any plans to standardise? What percentage of the market do you supply and do you have any marketing agreements with other companies regarding colour coding? Do you have any comments to make about the colour coding question? An identical questionnaire was also sent to the British Standards Institution.

Results

All the questionnaires sent out were returned completed. The information supplied enabled us to compile a comprehensive list of intravenous cannulae currently available on the UK market (Table 1).

The great variety of both colours and gauge sizes is remarkable. Gauge sizes range from size 10 down to size 26, together with a wide spectrum of colours to differentiate them. Some companies (Wallace and Sherwood) have different types of cannulae, but colour the same gauge sizes differently. Colours such as orange and brown can be confusing and difficult to tell apart, while further confusion arises from different hues of the same colour (e.g. dark and light blue).

All companies agreed on the need to introduce a colour coding standard, and three were in favour of adopting the ISO 6009 hypodermic needle standard.[3] Surprisingly, six of the nine companies were unaware of any plans to standardise the colours, but three outlined the present situation. All companies emphasised the problem of getting everyone to conform to a single standard, but believed that the problems involved in conversion could be easily overcome. Most companies declined to give their market share figures, but the largest manufacturers of cannulae worldwide are Viggo (Venflon), Becton–Dickinson (Insyte), Critikon (Jelco) and Travenol (Quikcath), who do use a similar colour code.

None of the companies had any agreements between them about colour coding their cannulae.

Discussion

There is no colour coding standard in the United Kingdom at present. The only existing British standard is BS 4843 which defines sterility and packaging requirements but does not mention colour coding.[4] The International Standards Organisation have a colour code for single-use hypodermic needles,[3] but this code does not apply to indwelling intravenous cannulae. The only two colour code standards presently use are the French standard and the Swedish national standard. These are essentially the same and differ on only two colours.

The suggestion of using the ISO standard for hypodermic needles would not be practical since the gauge sizes are too small. A trade organisation called the Disposable Hypodermic and Allied Equipment Manufacturers Association of Europe (DHAEMAE) in March 1988 drafted a colour code based on the French national standard to be used as a basis for an international standard. (Table 2.)

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Table 1. Intravenous cannulae currently available on the UK market with their respective colour coding.

Gauge Size	Intraflux Intravalve (Vygon)	Venflon Vasculon (Viggo)	Abbocath (Abbott)	Quikcath (Travenol)	Medicut (Sherwood)	Mediport (Sherwood)	Angoicath (Deseret)	Insyte (Becton–Dickinson)	Wallace IV (Wallace)	Wallace YCan (Wallace)	Jelco (Critikon)	Braun (Braun)
10							White					
11									White			
12	Dark blue				Light blue		Orange		Pink	Light green	Orange	Orange
13	Red											
14	Orange	Brown	Green	Orange	Brown	Green	Pink	Orange	Yellow	White	Grey	Grey
15		Orange										Yellow
16	Grey	Grey	White	Grey	Grey	White	Yellow	Grey	Red (17.5)	Pink	Green	Green
17		Yellow							Green (18.5)	Light yellow		
18	Green	Green	Pink	Green	Green	Pink	Tan	Green	Light green	Dark green	Pink	Pink
19												
20	Pink	Pink	Yellow	Pink	Pink	Yellow	Green	Pink	Blue	Blue	Blue	Blue
21												
22	Light blue	Blue	Black	Blue	Dark blue	Black	Blue	Blue			Yellow	
23												
24		Lime	White	Yellow			Lavender	Yellow	Light yellow			

Table 2. Draft DHAEMAE standard specification for sterile single-use intravenous cannula units.

Gauge	Colour
26	Black
24	Yellow
22	Blue
20	Pink
18	Green
17	White
16	Grey
14	Orange
13	Red
12	Light blue

Table 3. The proposed colour code.

Gauge	Colour
24	Yellow
22	Blue
20	Pink
18	Green
16	Grey
14	Orange
12	White

Subsequently, the International Standards Organisation in June 1988 formed a working group with representatives from leading manufacturers and national standards organisations. Their aim is to draw up an international standard by October 1989, and they have agreed to consider the proposals put forward by DHAEMAE.

A standard should offer the consumer a fixed number of cannulae gauge sizes with an easily recognisable colour code. We have devised a colour code that is clear and simple and offers manufacturers the best compromise over cannulae already in production. (Table 3.) The seven gauge sizes each have a distinctive colour and will cover the majority of clinical situations. We consider this code to be more simple, less equivocal and avoids use of hues of the same colour, compared with the DHAEMAE proposals. It should be easy for manufacturers to introduce an extra size at either end of the spectrum without compromise to the existing format.

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Introducing patient-controlled analgesia for postoperative pain control into a district general hospital

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Summary

Patient-controlled analgesia was introduced in a district general hospital in order to improve postoperative pain control. Techniques of management were developed with effectiveness, safety and practicality as the main objectives. An analysis of the first 1000 patients to use the system is presented. Problems were encountered with slow respiratory rate, monitoring, equipment function and ward management. Identification of specific hazards and management problems led to improvements in system safety. Patient-controlled analgesia has become the standard technique for postoperative pain control after major surgery in this hospital.

Key words

Pain; postoperative.
Analgesia; patient-controlled.

Patient-controlled analgesia (PCA) has been used widely in the United States of America and in research units in the United Kingdom for some years and has an impressive record of safety[1–3] and of effectiveness[1,4] in the control of postoperative pain. The technique must be transferable to ordinary busy surgical wards in District General Hospitals (DGH) to benefit the majority of patients who undergo major surgery.[3] It must be effective and safe in an environment where levels of nursing staff and expertise may vary widely.

This paper examines the introduction of PCA at the James Paget Hospital, Great Yarmouth, a DGH of 560 beds, and its use over a 2.5-year period.

Methods

The PCA pumps used were Graseby Patient Controlled Analgesia Systems (PCAS, Graseby Medical, Watford, England). No printers were used except during an initial trial on seven patients. All hospital consultants were briefed about the technique at the conclusion of the trial period, and their cooperation was sought for its formal introduction. There were no objections. Sixteen pumps were put into service over the next 2 years.

The use of PCA was concentrated initially on three wards (two orthopaedic and one general surgical). This limited environment allowed anaesthetists and nurses to gain familiarity with PCA and to develop safe techniques for managing the system. PCA was introduced to the remainder of the wards after 100 patients had been treated.

Patients who had undergone major surgery were selected for PCA. Initially, those who could not understand the system or operate the pneumatic trigger were excluded. Later this policy was withdrawn. In most cases the pump was set up by the anaesthetist during the quieter moments of the operation. With familiarity this procedure could be performed in about 5 minutes. Intravenous access was gained either by way of the side arm of a one-way 'Y' connector incorporated into the main intravenous line or through a dedicated intravenous cannula. Diamorphine was chosen since it was readily available and commonly used for postoperative analgesia.

All pumps were programmed by anaesthetists. Standardisation and simplicity were believed to be important. Diamorphine concentrations of 1 mg/ml were suggested as the norm and pumps were charged with 60 ml of solution. Decisions as to bolus dose, bolus dose infusion rate, lockout time, and background infusion were left to the individual anaesthetist.

Pumps were usually activated either at the end of surgery or on arrival in the recovery ward. Recovery nurses supervised initial use of PCA by the patient and reinforced instructions on pain control given before operation. Each patient's vital signs were monitored in the normal postoperative manner after return to the general ward. Observations of respiratory rate were scheduled at 5, 10, 15, 30, 45, 60, 90 and 120 minutes after return. The anaesthetist was informed if it decreased below 10 breaths/minute but if it fell below eight then PCA was stopped and the anaesthetist was called to see the patient.

Nurses were instructed specifically to check patients and pumps at the regular 4-hourly drug round. The total quantity of opiate infused, the total number of boluses given and the total number of bolus attempts were read from the pump's display screen. A simple assessment of the patient's comfort was also made. Nurses were requested to assess pain on a scale of 0 to 4 (0–none; 1–mild; 2–moderate; 3–severe; 4–excruciating). All data were recorded on a custom-designed chart.

The anaesthetist who set up PCA remained responsible for initiation of any changes in the programmed regimen. Nursing staff were directed to communicate any problems to that anaesthetist, or if unavailable, to the duty anaesthetic team. Teaching of the technique was incorporated into the 'Extended Role of the Nurse' course and this enabled a large number of nurses to become familiar with the principles involved. Each ward that used the PCA was supplied with a Users' Manual produced by Graseby. In addition the authors produced their own 'Guide to PCA'. Nurses were neither taught nor expected to programme the pumps.

Results

The charts of 1000 patients were reviewed. PCA was used for a wide range of orthopaedic, general, vascular,

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Table 1. Details of patients who developed respiratory problems during PCA.

Case no.	Age (years)	Operation	Intra-operative opiate	Background infusion (mg/hour)	Bolus dose (mg)	Lowest respiratory rate	Hours after operation	Diamorphine received (mg)	Background discontinued	PCA discontinued	Total diamorphine in first 24 hours (mg)	Remarks
Slow respiratory rate—background infusions												
23	80	Colostomy	Fentanyl and papaveretum	0.5	1	6	5	12	Yes	12 hours	23	
84	74	Revision of total hip replacement	—	1	1	7	3	3	Yes	No	15	Breathing rate low over first 24 hours. Bolus reduced to 0.3 mg
129	65	Total hip replacement	—	0.5	1	7	7.7	15	Yes	No	29	Bolus dose reduced to 0.5 mg
195	74	Total hip replacement	Fentanyl	1	1	8	10	19	Yes	8 hours	21	
290	77	Total hip replacement	Fentanyl	0.5	1	5	3	14.6	Yes	1 hour	32	Returned to ward with respiratory rate of 8/minute
314	78	Cholecystectomy	Fentanyl	0.5	1	7	3.5	8.6	Yes	Yes	—	
347	56	Femoro-popliteal bypass	Papaveretum and fentanyl	0.5	1	6	1.5	4.9	Yes	2 hours	25	Opiate premedication. Respiratory rate 6/minute on arrival on ward
703	62	Cholecystectomy	Diamorphine	1	1	3	4	7.6	Yes	No	14	Naloxone used
931	81	Nephrectomy	—	1	1	8	2.5	N/A	Yes	No	Not available	Poor records. Possibly some respiratory obstruction. Naloxone used
Slow respiratory rate—no background infusion												
204	72	Revision of total hip replacement	—	0	1	8	11	26	—	1 hour	41	Awake and in pain. Given naloxone unnecessarily
459	63	Pyelolithotomy	Fentanyl	0	1	4	2.5	20	—	Yes	33	Doxapram at end of operation. Naloxone used. Intramuscular opiate after PCA stopped

Table 1. *Continued.*

Case no.	Age (years)	Operation	Intra-operative opiate	Background infusion (mg/hour)	Bolus dose (mg)	Lowest respiratory rate	Hours after operation	Diamorphine received (mg)	Background discontinued	PCA discontinued	Total diamorphine in first 24 hours (mg)	Remarks
511	55	Total hip replacement	Fentanyl	0	1	6	1.5	21	—	No	59	
673	55	Cholecystectomy	Papaveretum	0	1	7	4	11	—	No	19	Opiate premedication
766	71	Hip hemi-arthroplasty	Fentanyl	0	1	5	1.5	8	—	No	38	Fully awake
773	69	Cholecystectomy	Fentanyl	0	1	8	2.7	16	—	No	59	
903	42	Hysterectomy	Papaveretum	0	1	8	1	12	—	No	35	Awake and in pain
Slow respiratory rate before PCA started												
607	67	Laparotomy	Fentanyl	0	1	6	1	0	—	No	11	Opiate premedication
718	59	Cholecystectomy	—	0	1	4	0	0	—	5 hours	26	Opiate premedication. Slow respiratory rate in recovery area and on return to ward
Respiratory obstruction												
6	66	Total knee replacement	Diamorphine	1	1	—	2	3	Yes	Yes	3	Receding lower jaw. Previous history of 'opiate sensitivity'
124	76	Total hip replacement	Diamorphine	0.5	1	—	2	3	Yes	No	8	'Acromegalic type' jaw (but not a true acromegalic)
298	73	Total hip replacement	—	1	0.5	—	2	1	Yes	No	7	Receding lower jaw. Partial airway obstruction when somnolent
827	76	Total hip replacement	—	0	1	6	4	12		No	30	Obstructive respiration with sleep. Fully rousable
Miscellaneous												
117	75	Total hip replacement	—	1	1	—	12	20	No	No	79	Chronic obstructive airways disease. No peri-operative treatment
169	76	Revision of total hip replacement	Papaveretum	1	1	4	15	20	Yes	Yes	—	'Y-Connector' misplaced. Diamorphine pooled in the intravenous line
192	66	Revision of Hartmann's procedure	Fentanyl and diamorphine	0	2	3	1	12	—	No	19	Large boluses encouraged in recovery ward. Bolus reduced on general ward

gynaecological and obstetric surgery. The ages of patients ranged from 5 to 93 years. No significant changes in anaesthetic practice occurred to accommodate PCA. The use of intra-operative opiates was common (68.5%) as was the use of regional anaesthetic techniques (31%).

The concentration of diamorphine used ranged from 0.5 mg/ml to 10 mg/ml, but 1 mg/ml became the norm for most patients. A range of bolus doses was used initially but 1 mg evolved as the standard adult dose. The initial bolus dose was adjusted as necessary according to the response of the patient. The initial bolus dose was decreased in 14 of the final 400 patients in the series and increased in six. The bolus dose infusion rate was always set at 100 ml/hour. The lockout time was set at 3 minutes for 62% of patients, 4 minutes for 12.2% and 5 minutes for 25%. A background infusion was used in 98 of the first 100 patients. However, anaesthetists changed their practice as experience grew and the frequency of use of a background infusion decreased to 13% in the last 400 patients. A wide range of infusion rates was used but 1 mg/hour and 0.5 mg/hour were the most popular. The average duration of PCA use per patient increased over the period of this study because of an increasing availability of pumps. The usual duration was between 36 and 48 hours; the longest was 232 hours.[5]

There was a wide variation in opiate requirement.[6-8] The largest quantity of diamorphine used during the first 24 hours was 572 mg. The quality of analgesia obtained was assessed from the records of 908 patients (pain assessment was not included at the start of the study). The nurses recorded little or no pain in 622 (68.5%) patients, one or more episodes of moderate pain in 220 (24.2%) and one or more episodes of severe or excruciating pain in 66 (7.3%). The episodes of moderate or severe pain occurred usually during the first few hours after operation. A total of 8170 assessments of pain were made and patients were reported as having little or no pain on 92.6% of occasions.

Respiratory problems occurred in 25 patients (Table 1). The respiratory rate of nine patients who received a background infusion combined with PCA decreased to 8 breaths/minute or less and PCA was stopped whilst an assessment was made. All patients subsequently made uneventful progress. The respiratory rate of seven patients who did not receive a background infusion decreased to 8 breaths/minute or less. Five patients were given no specific treatment and six continued to use PCA satisfactorily. Two patients developed a slow respiratory rate before starting to use PCA. Both had received opiate premedication. In one patient (number 169) the intravenous infusion was connected to the wrong limb of the one-way 'Y' connector and was not protected by the one-way valve. The respiratory rate decreased to 4 breaths/minute. $Paco_2$ was 6.18 kPa and Pao_2 15.76 kPa (on supplementary oxygen). No specific treatment was necessary after correcting the intravenous connections.

Problems encountered with pumps and connector systems are shown in Table 2. The most serious problem occurred when a PCA pump began to administer boluses independently of the patient trigger. This incident was traced to two early design faults which have since been corrected.

The two most common problems were related to the bolus triggers and the power cables. The trigger mechanism was inclined to 'prolapse' from the surrounding casing, especially when dropped on the floor and the power cables developed a tendency to work loose with regular use. This could lead to deprogramming of the pump when it or the patient was being moved. Deprogramming could occur also when the power cable was disconnected from the base of the pump without first switching off at the mains wall socket. The cause was identified as power surges from arcing within the pump socket. Misconnection of the 'Y' connector occurred twice and one brand of connector had to be withdrawn when the one-way valves proved faulty.

Table 2. Problems associated with the equipment used to deliver PCA.

Equipment problems	Number
Self-triggering	1
Trigger mechanism dislocation	Several
Deprogramming	29
Battery drained, power cable missing	2
Key switch failure	2
Software failure	2
Display board failure	1
Fuse blown	1
Battery failure	1
Casing fractured when pump dropped	2
'Y' Connector misplaced	2
'Y' Connector not 'one-way'	2

Table 3. Failures in the management of PCA on the wards.

Monitoring and instruction failure	Number
Monitoring inadequacies	Common
Supplementary analgesics	2
Nonanaesthetist interference	3
Pump not switched on	1

Table 4. Postoperative problems not directly related to the use of PCA.

Problems unrelated to PCA	Number
Hypovolaemia	*
Myocardial problems	6
Brain stem infarct	1
Masked urinary retention	1
Sedation from premedication or antiemetics	2
Urticarial rash	1

*Many episodes not recorded on the monitoring charts.

Problems with management of the PCA system on the ward are shown in Table 3. There were frequent failures in carrying out basic monitoring. An initial survey of 280 charts showed that only 119 (42.5%) were completed satisfactorily and that 69 (24.6%) had major inadequacies. The main failures were in monitoring breathing as scheduled for the first 2 hours on the general ward and in monitoring PCA during the daytime. Nurses in charge were held responsible for such failures. A subsequent survey of 398 charts showed an increase in satisfactory charts to 56.5%.

There were occasional failures by nurses and doctors to comply with our clear instructions with regard to the assessment of problems or the administration of supplementary analgesics. Untutored enthusiasts during the first few months would fiddle with the pumps and even attempt reprogramming. Interference with the programming by anyone other than anaesthetists was subsequently prohibited.

The major complications unrelated to PCA are shown in Table 4. Postoperative hypovolaemia after major surgery was encountered and prompted caution with PCA. The six recorded episodes of significant myocardial ischaemia included three fatalities. PCA was not implicated as the causative factor of any of these events.

Discussion

Most nurses welcomed PCA. Some needed frequent reassurance with patients who were perceived as 'using the PCA trigger too often'. Others mistakenly considered that the patient could not receive an overdose if the nurse herself activated the bolus trigger; this misconception was corrected promptly. Some anaesthetists required help with the use of the pump and with resolution of problems that occurred on the ward. We found that most patients readily understood the idea of PCA as explained at the visit before operation. Enquiries about safety and the possibility of self-overdose were common. No patient expressed any concern over being attached to a computerised pump. However, a patient-orientated leaflet on PCA would be useful.

We originally excluded specific categories of patient (those unable to use the trigger or comprehend the technique), although we soon realised that almost any patient can have the benefit of PCA, if the pump is operated by 'Proxy'. The proxy is a nurse or even a relative who operates the trigger to deliver a bolus provided that the patient either requests a bolus or expresses pain in some other way. We made no attempt to evaluate the Graseby PCAS beyond outlining the problems encountered with the pump. Programming appears relatively easy at first glance, but safe programming requires full comprehension of the concept of PCA and the function of the pump, as well as supervised initial practice. We decided that only anaesthetists should programme the pumps, prescribe the analgesic regimen, and alter management. Thus control of, and responsibility for, PCA rested in the hands of a small group of doctors. The choice of diamorphine as analgesic has proved satisfactory in our hands. It acts rapidly[9] and we found no problems that could be attributed specifically to the use of this opiate.

Safe management of PCA on general wards was considered to be the key to the successful introduction of the technique. We worked hard to develop an adequate monitoring programme but considerable effort is required to ensure the maintenance of a satisfactory standard. We have not yet succeeded in the introduction of monitoring of sedation, nausea and vomiting.

We selected breathing frequency as the most appropriate method of assessing respiratory adequacy, although we accept that this does not always reflect ventilatory depression. No other technique is used routinely on the wards of our hospital. PCA would fail if there were either significant respiratory problems associated with the technique or if the burden of monitoring became excessive. Patients are always closely observed in the recovery ward for any respiratory embarrassment, and are often stimulated by various manoeuvres. In contrast, they usually receive less observation and stimulation after arrival on the general ward. Consequently, we introduced a specific schedule for monitoring the rate of breathing during the first 2 hours on the ward.

The use of background infusions diminished when we identified associated problems (Table 1). PCA is at its safest when used alone as a demand system. A background infusion fixes a mandatory analgesic intake and since it is impossible to predict any patient's absolute requirement,[10] some patients are likely to receive an excessive dose.[11,12] We considered the incidence of slow ventilatory rate associated with the use of background infusions (2.5%) to be unacceptably high. If continuous opiate infusions are used routinely then respiratory depression will occur in some patients. Ray and Drummond[11] stopped infusions of morphine in 28.7% of their patients because of slow breathing rate. Patients who require high doses of opiates postoperatively are probably managed more safely and effectively with larger bolus doses rather than infusions. An argument against the demand mode is that the patient may be unable to sleep because of the need to administer boluses.[13] None of our patients complained of this.

Others have analysed in depth the quality of the analgesia produced by PCA.[1,4,7,14–16] However, these types of analyses are either inappropriate or very difficult to implement in a busy DGH. Our analysis is crude. However, only 29% of patients complained of episodes of significant pain and only in 8.2% was pain severe. These results are comparable to those achieved by others.[4,16] A systematic record of patients' evaluation of the technique would have been useful.

We found a natural tendency amongst staff to blame the new technique of PCA for a wide variety of routine postoperative complications. A critical analysis of these as well as adequate standards of monitoring and record keeping are essential so that the technique does not fall into unjustified disrepute. Medical audit will encourage this.

The alarming incident in which one of our pumps delivered analgesia without being triggered underlines the importance of rapid correction of known faults in equipment. One of the faults related to this episode had been previously identified[17] but was not rectified. The pumps were found to 'fail safe' in all other situations. The use of a one-way 'Y' connector to connect PCA to an intravenous infusion is mandatory and the use of specifically designed integral 'Y' infusion sets which incorporate one-way and antisiphon valves improves safety.

All unauthorised manipulation of the pumps and their programming by the inexperienced must be prohibited (other than switching the system off in an emergency). Similarly the use of other drugs that are significant central nervous system depressants must be barred.[18] Any such administration must be made by a doctor with experience in PCA. All staff must be instructed properly in their roles if disasters are to be avoided.

Hypovolaemia is, in theory, a situation in which PCA should be useful. The administration of small intravenous bolus doses of analgesic is the standard method of pain relief in the shocked patient. It has become our policy to continue PCA in such circumstances although it may be necessary to reduce the size of the bolus dose. However, Tamsen[19] believes that PCA is contraindicated in manifest hypovolaemia. As experience with PCA for postoperative pain control has grown in this hospital, so has its use for the control of other forms of severe acute pain associated with malignancy, major trauma, fractured ribs, renal colic, pulmonary embolism, labour and other circumstances.[5,20]

Conclusions

PCA has been introduced satisfactorily into our hospital. We have found it to be a simple, versatile and effective method of postoperative pain control, welcomed by patients, nurses and doctors. Its introduction requires careful planning and must include a comprehensive training programme for all relevant staff. Initially, programming and prescribing control should remain in the hands of a small group of individuals. We are satisfied that with simple management and monitoring techniques there is a high level of safety in PCA when used without a background infusion.

Acknowledgments

The introduction and evolution of PCA in this hospital has involved the whole Department of Anaesthetics in addition to the Recovery and Surgical Ward Nursing Staff. The authors acknowledge the contributions made by all concerned. A grant from the East Anglian Regional

Research Committee helped in the preparation of this paper. Finally, the role of the local people of the Great Yarmouth and Waveney Health District in raising funds for 14 of the PCA pumps must be applauded.

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Anaesthesia, 1990, Volume 45, pages 406–408

Postoperative analgesia in children who have genito-urinary surgery

A comparison between caudal buprenorphine and bupivacaine

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Summary

A study conducted on 40 children, aged 1–11 years, who had genito-urinary surgery compared the quality and duration of analgesia after caudal blocks in two groups of patients. Group 1 (n = 20) received caudal bupivacaine 0.25% and group 2 (n = 20) caudal buprenorphine 4 μg/kg; each received 0.5 ml/kg body weight. Patients were operated on under general anaesthesia. Postoperative behaviour and severity of pain were measured on a 3-point scale. The results indicate that caudal buprenorphine provides excellent postoperative analgesia in children comparable to caudal bupivacaine in the early postoperative period. Buprenorphine proved better in the late postoperative period. Analgesia lasted from 20 hours to more than 24 hours after caudal buprenorphine with fewer side effects.

Key words

Analgesia; postoperative.
Anaesthetic technique; caudal epidural.

Genito-urinary surgery causes considerable pain in children after operation and may lead to restlessness and agitation, with potential disturbance of the operative site. Caudal block is a satisfactory method of complete pain relief in such cases.[1,2] Caudal block with bupivacaine is more effective than intramuscular morphine[3] and is as effective as caudal morphine[4] in the treatment of postoperative pain after genital operations in children.

A single dose of intramuscular buprenorphine was used in children for postoperative analgesia and compared with caudal analgesia after circumcision.[5] Intravenous buprenorphine was shown to be a safe postoperative analgesic in young children.[6,7] Studies on compatibility with tissue and cerebrospinal fluid indicate that buprenorphine may safely be administered epidurally.[8] Most investigators have concluded that buprenorphine, when given via the epidural

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Table 1. Details of patients and operative time.

	Age (years)	Sex (M/F)	Weight (kg)	Operative time (minutes)
Group 1				
Range	1–11	20/0	7–22	15–90
Mean (SD)	4.6 (2.7)		13.8 (4.6)	42.5 (28.4)
Group 2				
Range	1–10	19/1	5–25	15–95
Mean (SD)	5.1 (3.1)		13.6 (5.3)	46.7 (30.1)

route in adults, provides safe and effective postoperative analgesia and would be more useful than epidural morphine.[9–11]

The present study compared the quality and duration of postoperative analgesia provided by caudal buprenorphine and bupivacaine in children who had genito-urinary surgery.

Material and methods

Forty healthy children, aged 1 to 11 years, admitted for genito-urinary surgery were included in the study (21 circumcisions, 15 hypospadias repairs, three urethrolithotomies and one vesicovaginal fistula repair). The nature of the study was explained to the parents and written consent obtained. The patients were divided equally into two groups. No premedication was given. All cases were operated on under general anaesthesia. Induction of anaesthesia was with thiopentone 5 mg/kg intravenously or by inhalation of nitrous oxide, oxygen and halothane. Anaesthesia was maintained with 66% nitrous oxide, oxygen and halothane (1–1.5%) through a facemask using a Bain coaxial system or Ayer's T-piece with spontaneous ventilation. An intravenous cannula was inserted and 5% dextrose infused. All caudal blocks were performed by one of the authors (S.K.) after induction of general anaesthesia, before the start of surgery. The area was cleaned and draped after the child was placed in the left lateral position with hip and knee joints flexed to 90°. The sacral cornua were identified and the sacrococcygeal ligament pierced with a 23-gauge needle. The analgesic solution was injected after an aspiration test for cerebrospinal fluid and blood proved negative. The injection rate was 0.5 ml/second.

Patients in group 1 received 0.25% bupivacaine and in group 2 buprenorphine 4 μg/kg body weight; the volume injected was 0.5 ml/kg body weight. The concentration of volatile agent was reduced towards the end of surgery so that the child made rapid recovery to consciousness after the operation. The patients were allowed to recover with minimal disturbance. Paracetamol (10 mg/kg) was prescribed as a postoperative analgesic and was given as required at the discretion of the nursing staff, who were unaware of the group allocation of the patient. The intravenous cannula was removed when the child was awake. Oral fluids were permitted as soon as requested by the child.

Table 3. Postoperative behaviour at 1, 2, 4 and 8 hours postoperatively.

	1 hour		2 hours		4 hours		8 hours	
Behaviour	1	2	1	2	1	2	1	2
Calm and cheerful	19	20	20	20	16	20	12	20
Restless or tearful	1	0	0	0	4	0	8*	0

*$p<0.01$ compared to group 2.

Table 4. Postoperative complications.

	Group 1 ($n=20$)	Group 2 ($n=20$)
Nausea and vomiting	6	4
Sedation	0	15*
Urinary retention	0	0
Sweating	0	1
Pruritus	0	0

*$p<0.001$ compared to group 1.

The children were assessed for postoperative behaviour and pain after return to the recovery ward by one of the authors (S.G.), who did not know to which group the patient was allocated. Assessments of postoperative behaviour took place at 1, 2, 4 and 8 hours after operation, and pain was assessed in the immediate postoperative period (0 hour) and 2, 4, 8 and 24 hours thereafter. The observer scored pain with reference to a 3-point scale (none or insignificant, moderate, severe) and behaviour similarly (cheerful and calm, restless, tense or tearful). Side effects such as nausea, vomiting, sedation, urinary retention, sweating and pruritus were recorded for 24 hours. Pulse rate, blood pressure and respiration were also monitored. The study concluded after 24 hours.

The data were analysed using Chi-squared test with Yates' correction, and Student's *t*-test wherever applicable.

Results

Patient and operative data. The two groups were comparable for age, sex, weight and operative time with no statistical differences (Table 1).

Pain evaluation. Satisfactory analgesia was defined as no pain reported, or insignificant pain and was achieved in both the groups in the immediate period after operation (0 hour) and at 2 and 4 hours (Table 2). All the patients in group 2 and 40% in group 1 had satisfactory analgesia at 8 hours after operation ($p < 0.001$) and 90% in group 2 and 55% in group 1 had adequate analgesia 24 hours after operation ($p < 0.05$). Analgesia lasted from 20 to more than 24 hours with buprenorphine and from 4.15 to 5.25 hours with bupivacaine (mean 4.40 hours).

Table 2. Number of children with pain in each group immediately after operation (0 hour) and at 2, 4, 8 and 24 hours thereafter.

	0 hour		2 hours		4 hours		8 hours		24 hours	
Pain	1	2	1	2	1	2	1	2	1	2
Moderate	0	0	0	0	1	0	7	0	3	2
Slight	2	1	0	0	4	0	5	0	6	0
None	18	19	20	20	15	20	8*	20	11†	18

*$p<0.001$ compared to group 2; †$p<0.05$ compared to group 2.

Postoperative behaviour. The two groups were comparable at 1, 2 and 4 hours postoperatively (Table 3). All patients in group 2 and 60% in group 1 were calm and cheerful at 8 hours after operation ($p < 0.01$).

Postoperative complications. Sedation was a common feature with caudal buprenorphine. Nausea and vomiting were similar in both groups (Table 4). One patient had sweating in the postoperative period in spite of the recovery ward being cool and comfortable. This child had no other complication. There was neither pruritus nor urinary retention. Pulse rate, blood pressure and respiratory rate remained stable throughout the study period.

Discussion

The results of this study indicate that both caudal buprenorphine and bupivacaine provide good analgesia in the immediate postoperative period but analgesia lasts longer after buprenorphine.

It is important that postoperative discomfort is relieved in order to minimise the stress and upset that arises from pain for both patient and parent. The caudal approach to the epidural space for anaesthesia and analgesia has been extensively used in children.[12] Caudal analgesia results in rapid return to normal activity, excellent analgesia in the immediate postoperative period and cardiovascular stability. Kay[1] used caudal bupivacaine to provide intra- and postoperative analgesia for circumcision. The use of epidural opiates for control of postoperative pain has achieved widespread recognition and acceptance in adults.[9,13] The use of epidural opiates via the caudal route in children, has mainly been described using morphine.[4,14] It was found to be as effective as caudal bupivacaine in the treatment of postoperative pain after genital operations with analgesia lasting from 10 to 36.5 hours.[4]

Buprenorphine was shown to be a useful analgesic in adults and children.[5,6,9,15] Its high lipid solubility and high affinity for opioid receptors suggest that it may be better than morphine for epidural use. The epidural dose of buprenorphine in adults varies between 0.06 and 0.3 mg;[10,16] best results are achieved with 0.3 mg and duration of action from 12[10] to more than 24 hours.[17] We decided to use buprenorphine 4 μg/kg body weight epidurally via the caudal route; the dose was calculated according to the effective dose of 0.3 mg in adults.

The assessment and quantification of postoperative pain in children is difficult. Therefore, the observer's assessment based on the behaviour of the child is necessary. The duration of caudal block with bupivacaine agreed with the duration reported by others.[4,18,19] The analgesia offered by caudal buprenorphine was comparable to caudal bupivacaine in the early postoperative period. However, buprenorphine was better than bupivacaine in the late postoperative period.

The incidence of complications with caudal bupivacaine was similar to that previously reported.[4,19] Nausea and vomiting were similar in both groups. Studies with epidural buprenorphine in adults have also shown a low incidence of nausea and vomiting.[11] Sedation was seen in 75% cases with caudal buprenorphine. It is not always possible to distinguish sedation from analgesia in children, and the greater sedative effect of buprenorphine might be mistaken for analgesia in children who fall asleep. One child sweated late in the postoperative period; this was seen in 2–12% of cases with buprenorphine.[20]

In conclusion, caudal buprenorphine 4 μg/kg body weight provides excellent postoperative analgesia in children who have genito-urinary surgery. It is as effective as caudal bupivacaine 0.25% in the early postoperative period but in the late postoperative period provides better analgesia than bupivacaine.

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Resuscitation procedures

The following comments are based on personal knowledge, as the medical adviser to the Fatal Accident Enquiry conducted by Sheriff Lockhart, which was mentioned by Dr P.J.F. Baskett and his colleagues in their recent letter (*Anaesthesia* 1990; **45**: 62–3).

They quote the recommendation of the Resuscitation Societies that defibrillation is the priority treatment of ventricular fibrillation in patients who are 'reasonably well oxygenated'. Prompt defibrillation whilst the patient's lungs were ventilated with expired air was preferred to initial intubation and ventilation with 100% oxygen in the particular case which they mention. The resuscitation was unsuccessful. Some 20 minutes later, after transfer to the Royal Hospital for Sick Children the child's trachea was intubated, the lungs ventilated with oxygen and the heart defibrillated with restoration of cardiac output and resumption of spontaneous ventilation. The cerebral damage was profound and progressive and she died later. The failure of the initial defibrillation in a previously healthy child was, to me *prima facie*, poor oxygenation. It

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was inexplicable for a professional anaesthetist to abandon his machine with its supply of oxygen, ignore the availability of a laryngoscope and tracheal tubes in favour of expired air ventilation, using a Brook airway, by his dental colleague. Laryngoscopy alone would have ensured a clear airway after the surgical procedure and, in the circumstances where a defibrillator has to be sought, the child's clothing removed or displaced and a diagnosis established, a professional anaesthetist could easily have intubated the patient. This would have enabled any assistant to ventilate the patient with 100% oxygen which would have materially improved the chances of a successful defibrillation and would have imposed little or no delay in applying the countershock.

Experience of three separate instances of ventricular fibrillation which occurred during chairside dental anaesthesia in Glasgow Dental Hospital and School in patients who were continually monitored with an ECG supports the view that prompt defibrillation after ventilation with 100% oxygen is a rewarding exercise.

A case for immediate countershock can be sustained for a patient who is in a CCU or undergoing cardiac investigation, lightly clad, being continuously monitored and with a defibrillator to hand.

The Sherriff was sympathetic to the problems of the single-handed anaesthetist working in isolated locations. His recommendations were specifically directed to such individuals working in dental surgeries or community clinics and his conclusions were, I believe, well founded.

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Anisocoria in cardiopulmonary bypass

The reports of normal pupil response during hypothermic cardiopulmonary bypass (CPB) are sparse and we welcome the data provided by Woodall *et al.* (*Anaesthesia* 1989; **44**: 885–8). We were surprised to learn of their finding of anisocoria in 23% of cases. These results are different from those of a similar study[1] of 127 patients, anaesthetised with sufentanil, etomidate, pancuronium, oxygen–air, and oxygenated on CPB with a membrane oxygenator. Pupil size was measured with a gauge similar to that used by Woodall *et al.*, but calibrated in French gauge (1 Fr. = 0.34 mm) which enabled detection of more subtle changes in pupil sizes. Pupil diameters were measured over the range 17.7 to 37.6°C in the adult group ($n = 99$) and 16.4 to 37.8°C among infants ($n = 28$). Anisocoria occurred temporarily only in one adult (1%) and in three infants (0.7%), but on these occasions the temperature was less than 25°C, in both adults and infants. Pupillary diameter increased with hypothermia in both adults and infants, but only at temperatures under 22°C was pupillary diameter increased to beyond normal limits (>6 mm). There were no neurological sequelae among these patients.

These differences may be a reflection of the different populations, other bypass techniques or anaesthetics used, so we are interested in the explanation of Woodall *et al.* for their frequent finding of anisocoria. Some further questions remain. Were they able to relate the finding to a particular operative event? Did they note an association with temperatures under 25°C? Was anisocoria more frequent among infants or those who did not receive high dose opiates? If, as Woodall *et al.* suggest, anisocoria is more frequently associated with neurological complications, then its finding is pathological and it should be sought in all patients undergoing CPB. The question remains, however, what intervention if any do they take when a patient develops anisocoria?

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Reference

1. HUET RCGG, KARLICZEK GF, COAD NR. Pupil size and light reactivity in hypothermic infants and adults. *Intensive Care Medicine* 1989; **15**: 216–7.

A reply

Thank you for the opportunity to reply. There were, as they suggest, differences in patient population: 7% of our cases were children, whereas 27% of the patients studied by Huet were infants. The techniques of anaesthesia, including the use of nitrous oxide, were different, perhaps also the surgery, and the degree of cooling required. Pierce and Huet confirmed in their letter one of our findings, that anisocoria may be transient; as it was in each of the four cases we described. We examined our patients at six different stages during surgery. It is clear from their letter published elsewhere that Huet, Karliczek, and Coad[1] made observations twice during some of their study cases. Anisocoria may not have been noticed by them.

No association between lower temperature on bypass or the anaesthetic technique and anisocoria was noted by us, but this may reflect the small number of our patients who were cooled to less than 25°C or who received high dose narcotics.

We found inequality of pupil size was associated with postoperative neurological dysfunction, but it was also a relatively common finding; 23% of our patients developed anisocoria at some stage, and most of them recovered from surgery uneventfully. Pupillary observation may complement other forms of monitoring used during cardiopulmonary bypass and may be useful in timing the intraoperative events which lead to neurological dysfunction, but this remains a subject for further study.

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Epidural or general anaesthesia for Caesarean section?

Evans, Murphy, Gray *et al.* (*Anaesthesia* 1989; **44:** 778–782) raise some very important issues in their excellent article that compares epidural versus general anaesthesia for elective Caesarean section and their effect on the neonatal Apgar score and acid-base status. They recommend an increase in the use of epidural anaesthesia for Caesarean section. This point of view is accepted by many obstetric anaesthetists. However, unless we are prepared actively to encourage *all* parturient women to undergo Caesarean by epidural anaesthesia a persistent group of mothers will remain, who are unwilling or unable to deliver using this technique. These mothers will deliver under general anaesthesia, accompanied by the consequent disadvantages to the neonate outlined in this article. Encouragement to the majority of mothers to undergo Caesarean section by epidural anaesthesia reduces the number of neonates whose condition at birth is suboptimal, but it does not address the heart of the problem, namely, the inadequate manner with which the talents of the paediatricians are utilised as a result of their poor training.

We wholeheartedly agree with their observation that neonatal resuscitation is not without risk. Iatrogenic laryngospasm, trauma to the upper airway, pneumothorax and tracheal perforation are the hazards they mention. Every anaesthetist who has participated in a delivery by Caesarean section will appreciate the irritation and frustration caused when neonates who emerge with a lusty cry, subsequently are the unwitting recipients of desperate attempts at intubation by an inexperienced paediatric SHO, often unaware of the difference between the sedated and the asphyxiated neonate. Insufficient distinction is made in this article between these two conditions, namely the transient influence of nitrous oxide or the volatile anaesthetic agents and prolonged hypoxaemia.

Rather than press for the expansion of epidural anaesthesia by maternal coercion in order to avoid the potential hazards of neonatal resuscitation the emphasis should, without any shadow of doubt, be on better training and supervision for the paediatrician. The paediatrician responsible for neonatal resuscitation should not be the itinerant vocational trainee or similar person, but an experienced individual, who can distinguish between the neonate who should be left alone to excrete the gaseous anaesthetic drugs and the neonate who requires active resuscitation.

The 1-minute Apgar score has misled us for 20 years, and has led to a high incidence of maternal awareness during Caesarean section. No study has demonstrated that poor Apgar scores at 5 minutes, which may be attributed by default to general anaesthesia, result in long-term detrimental outcome for the fetus any more than general anaesthesia in neonates does. The Apgar scoring system at 1 minute should either be abandoned, or we must redefine the acceptable limits in neonates born under maternal general anaesthesia.

The American collaborative study of perinatal outcome 1959–66 found that the Apgar score was insensitive as a predictor of neurological outcome; 73% of the infants who were later diagnosed as suffering from cerebral palsy had Apgar scores of 7 or above at 5 minutes.

Ruth and Raivio[1] followed up infants born with low Apgar scores and acidosis. They also commented on the poor correlation between the Apgar score and neurological outcome, even when taken at 5 minutes. Their own study clearly demonstrated that the 5-minute Apgar score was too insensitive a test to identify more than 12% of asphyxiated neonates and further had little predictive value. However, they still contend that the 5-minute score can be a useful tool. The 1-minute score is no use for this purpose. The significance of the Apgar score in relation to neonatal outcome is thus far from clear-cut. We should be cautious in modification of our anaesthetic practice in response to so imprecise a measure of outcome; rather we should improve the training of paediatricians.

We have been misled in the past by the 1-minute Apgar score after maternal general anaesthesia. We will be misled again unless we re-evaluate its significance in relation to sedation rather than asphyxia.

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Reference

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A reply

We thank Drs Lawes and Goodrum for their kind observations. They make important points.

Resuscitation of the newborn is undoubtedly generally not carried out as effectively as it should be anywhere in the world. For that reason the College of Anaesthetists, Royal College of Obstetricians and Gynaecologists, British Paediatric Association and Royal College of Midwives have jointly issued training programmes in basic and advanced resuscitation which should lead to improvements.[1] However, there is surely no doubt that at present the need for treatment introduces a hazard which may be of substance.

Differences between the sedated and asphyxiated infant are of limited importance. It is practically impossible for even a very experienced paediatrician to distinguish, on clinical grounds alone in the severely depressed infant within minutes of delivery, between the depressive effects of anaesthetic agents and those of asphyxia. It would be sheer folly to leave such an infant alone to see if it were merely sedated, and likely to be capable of excreting the gaseous anaesthetic drugs to which it had been exposed, possibly to recover spontaneously. Such babies require immediate attention irrespective of the cause of their depression, since a continued absence of effective ventilatory effort will inevitably lead to the biochemical consequences of asphyxia.

We are aware that the Apgar score has a poor correlation with ultimate outcome. However, using the Apgar score in broad categories showed that there was a real difference between techniques which lead to the need for resuscitation procedures. Clearly epidural anaesthesia is better in that respect and anaesthetists will note that. This does not mean that general anaesthesia must be abandoned, but the reasons for the differences, drug depression and (or) asphyxia, must be investigated and, if possible, corrected. At present we are attempting to tackle some of these problems.[2,3]

These are indeed complex issues and we are grateful for another opportunity to explain them to clinicians.

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The interpretation of results by doctor technicians

Measurements performed by ITU stat-labs have expanded considerably, and now include not only measurements related to 'oxygenation' (the 'blood gases', together with haemoglobin, haematocrit, oxygen saturation, carboxyhaemoglobin, and methaemoglobin), but also blood chemistry including sodium, potassium, calcium, glucose, urea, and albumin. Previous editorial comment[1] has highlighted the advantages and mentioned the dangers of ward-based, nontechnician operated, laboratory investigations. A recent Department of Health circular about blood gas machines has emphasised the dangers, and could lead to re-evaluation of ward based stat-labs, unless proper (and mandatory) quality control procedures, and operator training is pursued. Training may be difficult, but not impossible with a large and potentially fluctuating operator group. Individual sample quality control will be impracticable, or not practised, so that operator error (despite training) will go unnoticed and unsuspected.

Anaesthetists should be well aware of the pitfalls of blood gas measurement, although others may not be so well versed: not all blood gas machine users know the value of the alveolar air equation in checking the validity of their results, or of the importance of sample collection and preparation (time, temperature, bubbles, sample mixing, excess heparin in microsamples etc).

Sodium and potassium used to be measured using flame photometry (and were technically difficult for the doctor–operator technician). Now, however, ion electrode technology has allowed much easier and more reliable measurement of these (and other) ions, and doctor-technicians may not be aware of some of the problems. Thus, for instance, ionised calcium may be available as a 'bonus' in machines purchased primarily to measure another ion for example, potassium (as is the case in this ITU).

We have assigned little clinical credence to the result because of the known effect of blood pH upon ionised calcium, and the variable effect of heparin upon ionised calcium (which it binds).[2,3] The recent DoH warning has led us to review this problem in more detail, particularly since we know this machine is now used by non-ITU doctors. We have measured ionised calcium in blood taken for arterial blood gas analysis (sodium-heparin anticoagulant) and that which was taken from the same arterial line at the same time but anticoagulated conventionally in lithium-heparin. We have also measured calcium in blood similarly anticoagulated, but taken from a venous line. The measurements are compared with those obtained from venous 'clotted' (unheparinised), separated specimens, taken free-flowing. We regard this as the standard. The results are sufficiently different to alter therapy (see Table 1). Mean ionised calcium in blood taken for arterial blood gas analysis showed calcium to be 76% of our standard (0.86 and 1.13 mmol/litre). No pH 'correction' was applied: correction may, in any case, be improper.[3]

Table 1. Ionised calcium measurements in arterial and venous blood drawn from 10 consecutive patients (mmol/litre, mean, SEM): the effect of the anticoagulant.

Anticoagulant	pH	Calcium* mmol/litre (SEM)
Arterial		
Sodium-heparin	7.38†	0.856 (0.050)
Lithium-heparin		1.009 (0.055)
Venous		
Sodium-heparin	7.34†	0.859 (0.041)
Lithium-heparin		0.998 (0.046)
Clotted, separated		1.130 (0.061)

*Both sodium-heparin groups different from lithium-heparin groups ($p < 0.03$); both sodium-heparin groups different from clotted ($p < 0.002$); venous lithium-heparin group different from clotted ($p < 0.05$).
†No statistical difference.

We draw your readers' attention to these observations because of the increased availability of 'user friendly' machines in ITU stat-labs. Nontechnical operators (e.g. doctors) may use inappropriate samples for example, calcium. A significant delay in measurement will occur if samples are required to clot and then to be separated. There is an inevitable tendency for impatient users to use the 'blood gas' (sodium-heparin anticoagulant) for this measurement, and to assign the same 'accuracy' to the ionised calcium measurement as that afforded to the measurement of the blood gas, or the potassium.

Chemical pathologists are aware of the pitfalls of their machines and measurements, but less knowledgeable users (such as ourselves) are not so well informed. Even the most sophisticated, user friendly machines cannot cope with all operator or sampling errors. Interpretation of reliably measured blood gas results is suspect;[4] interpretation of unreliable measurements might be damaging.

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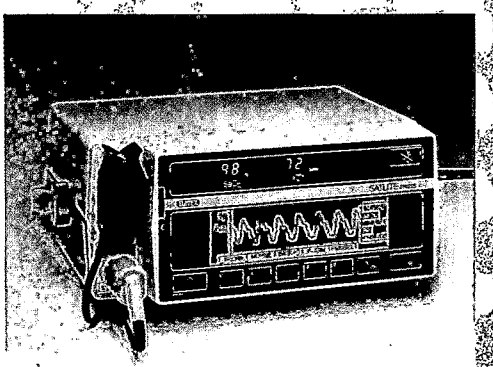

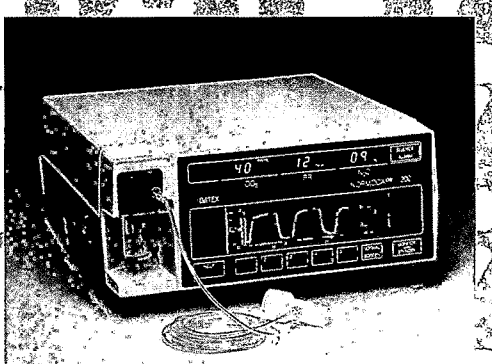

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Taking the sting out of postoperative analgesia in children

We wish to respond to the letter (*Anaesthesia* 1989; **44:** 1000–1) from N.G. Lavies and J.G. Wandless, about their trial in which a 23-G Wallace Y-Can was inserted subcutaneously, and used for injection of morphine sulphate after operation.

The intramuscular route would be far superior due to the poor distribution of drugs from subcutaneous tissue, and we would be interested to know the reasons for the choice.

We suggest that one cannot draw any significant conclusions from the study itself because it was too small, there was no control group, there was a large variation in the operations and the numbers were not sufficient to eliminate this variable, and the pain assessment methods were not valid or reliable.

It appears that there was no standardisation of the objective method used to assess pain. Various nurses carried out the assessments, so the scores were subjective for each individual nurse. There is also no mention of any guidelines for which behaviours to observe, or the timing of observations.

How was the 'patient acceptability' score attained? Only the person experiencing the pain could give information about this, and only one patient in the trial was old enough to do so!

The results of a projected randomised trial of intramuscular Y-Can and injections in 4- to 16-year-olds, using reliable subjective pain assessment methods will be published shortly.

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Subcutaneous narcotics

Drs Lavies and Wandless' (*Anaesthesia* 1989; **44:** 1000) letter about postoperative subcutaneous morphine states that 'computer search of the English literature revealed only three papers concerning this route of administration'.

Their computer, however, did not discover work on the use of continuous subcutaneous narcotics at our hospital. In the mid 1970s after much previous work Dr B.M. Wright in the Clinical Research Centre, Department of Bioengineering at Northwick Park Hospital designed a practical, efficient and cheap syringe driver.[1] This was first used extensively for iron administration to patients with thalassaemia but it created an opportunity for continuous administration of many substances. We began to use continuous intramuscular narcotics in 1978 and subsequently subcutaneous postoperative narcotics first with a cannula and later with a butterfly needle as described in a letter.[2] Dr Wright also mentioned this work to his own general practitioner, Dr P.S.B. Russell, who worked in the Michael Sobell Terminal Care Unit in Northwood, and he made a preliminary communication about its use.[3] The complexity of assessment of the success of this new analgesic method, despite much appreciation by patients, nurses and surgeons, ensured that our first report was delayed until 1985.[4]

We have noted extensive use of this practice and welcome its application to children, to whom continuous rather than intermittent administration may be preferable, provided correct charting is undertaken. The recording method we use seems particularly helpful.[4]

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Desmopressin and open heart surgery

We are sorry to see that Drs Bidstrup and Royston (*Anaesthesia* 1989; **44:** 1009) regard our letter (*Anaesthesia* 1989; **44:** 363) relating to desmopressin as prejudiced.

Our object, after a report on the usefulness of desmopressin in a patient with von Willebrand's disease, was to draw your readers' attention to its possible application after cardiac surgery. A very recent publication,[1] however, has concluded that the majority of patients who undergo elective cardiac surgery (mostly coronary artery bypass grafting) received no benefit from the use of desmopressin.

We considered, as an addendum to our letter, that a mention of the dramatic reduction in blood loss using aprotinin was called for. It should be said that its modest beneficial effect, reported almost 20 years ago,[2] was at a lower dosage than presently described and the vogue for its use then was more of an art than (today's) science.

Incidentally, the *British National Formulary* describes aprotinin as containing 100 000 k.i.u. in 5 ml of solution (not 10 ml) and advises an initial dose of one million k.i.u. for hyperplasminaemia, followed by 200 000 k.i.u. every hour until bleeding stops, despite the 0.9% benzyl alcohol preservative.

We wait with great interest for information on the cost, safety and optimum dosage of preservative-free aprotinin, for the purpose of reduction in blood loss during cardiac surgery where it clearly now has a place.

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Dosage volume or concentration?

Neither the use of 0.25% plain bupivacaine for spinal analgesia in adults nor the use of doses of less than 10 mg bupivacaine has received much investigation. Nielsen *et al.*[1] conclude that the use of 0.5% plain solution of bupivacaine confers no advantages over the 0.25% solution, and McClure *et al.*[2] suggest that the use of an adequate dose of local anaesthetic in a small volume gives a more predictable block.

An earlier randomised (as yet unpublished) prospective study of 51 patients for surgery for fractured neck of femur showed that adequate analgesia was produced by using either 3 ml 0.5% or 3 ml 0.25% plain bupivacaine (M.V. Achwal and H.G.R. Balmer, personal communication). A feasibility study was carried out to determine whether 1.5 ml 0.5% plain bupivacaine was a suitable agent with the same anaesthetic technique, (the patient lies on the unaffected side and injection is through either the L_{2-3} or L_{3-4} interspace with a 22-G needle). Twelve patients were studied, the block was deemed to be acceptable when analgesia (tested with an ethyl chloride spray) had extended to the T_{12} dermatome. A satisfactory block was achieved in 15 minutes in eight patients. None of these patients required further intra-operative analgesia or analgesia in the recovery room; the median height of the block was T_{10} (range T_7 to L_1). Analgesia had extended only to the L_1 dermatome by 15 minutes in the other four patients, and they were given a general anaesthetic. All required analgesia in the recovery room.

Bupivacaine 7.5 mg is an adequate dose for spinal analgesia for fractured neck of femur in a volume of 3 ml and not in a volume of 1.5 ml. This challenges the proposition that dosage is more important than volume or concentration in the control of the spread of local anaesthetic solutions in the cerebrospinal fluid.[3]

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Unilateral subarachnoid anaesthesia

Dr Armstrong (*Anaesthesia* 1989; **44:** 918–9) reports a case of unilateral subarachnoid anaesthesia with heavy bupivacaine involving the dependent side. This is a case report of unilateral subarachnoid anaesthesia with heavy bupivacaine where the nondependent side was blocked.

A 49-year-old healthy woman (weight 85 kg, height 160 cm) presented for left bunionectomy and fusion left second toe. Past medical history was unremarkable and physical examination normal apart from moderate obesity, a small jaw and several crowned teeth. She had no back problem and did not suffer from heartburn. She had experienced severe nausea after a previous general anaesthetic for similar foot surgery. A spinal anaesthetic was deemed appropriate.

The subarachnoid space was easily located with a 26-gauge spinal needle at the L_{3-4} interspace with the patient in the sitting position using a midline approach. Cerebrospinal fluid (CSF) flowed freely from the hub and 2.5 ml 0.5% heavy bupivacaine was injected slowly with the bevel directed to the left. Repeated aspiration produced CSF during and after injection. She was immediately placed onto her left side.

She noticed that her right leg was very heavy within 2 minutes and 10 minutes later she had a dense motor and sensory block up to T_4 on the right as tested by pinprick. No block was evident on the left even after a further 10 minutes. The operation was subsequently performed under a general anaesthetic using propofol 150 mg, fentanyl 100 μg, nitrous oxide, oxygen and enflurane and was entirely uneventful. Her arterial blood pressure was stable throughout.

One hour after the spinal anaesthetic was performed careful questions revealed some paraesthesiae between S_2 and S_5 on the left, but the right side remained densely blocked to T_4. Motor function was normal on the left, but she was unable to lift her right leg. Anaesthesia on her right side wore off gradually over the next 3 hours and the left-sided paraesthesiae disappeared after an hour. She was very nauseated, but there were no other problems and she was discharged 4 days later.

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Postspinal headache

We read with interest the excellent article by Rasmussen *et al.* (*Anaesthesia* 1988; **44:** 571–3) in which postspinal headache incidence was the random compared after-use of 20 or 25-gauge needles in elderly and young patients. The incidence of headache was significantly lower in elderly patients than in young patients. Nevertheless, the incidence of postspinal headache with the 25-G needle (12.6%) was, in our opinion, excessively high: in our own experience,[1] a 25-gauge needle causes a lower incidence of postspinal headache (<1%). More recently, in a study directed to evaluate the influence of 24 hours horizontal decubitus in the incidence of postspinal headache,[2] we found, again, a lower incidence of this complication than in Rasmussen's results (1.42%). As in Rasmussen's work, the possibility of postspinal headache was mentioned neither during the visit beforehand nor by the ward nurses. The patients and the

observers for postspinal headache were unaware of the needle size. The needle bevel was always orientated in a parallel fashion to the longitudinal dural fibres.

Labat recommended that subarachnoid block be performed with the needle bevel orientated parallel to the spine.[3] Recently, Norris and co-workers[4] demonstrated that the incidence of headache after accidental dural puncture with a 17–18 gauge Hustead needle was significantly lower when the needle bevel was orientated parallel rather than perpendicular to the longitudinal dural fibres (70% and <25%). It is believed that when the needle bevel is parallel the dural hole is narrow and the tendency for it to contract and close is greater.[5]

The low incidence of postspinal headache seen among our patients is supported by Mihic[6] who demonstrated a significant decrease when needle bevel was parallel to dural fibres (16% and 0.2%).

We agree with Dr Rasmussen's proposition that when spinal anaesthesia is indicated in young patients, a small gauge needle should be used, but we disagree with the postulate that thicker needles could be used in elderly patients 'if technical difficulties were expected by using a small diameter needle': better training may be preferred.

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Propofol in acute porphyrias

The case report by Weir and Hodkinson (*Anaesthesia* 1988; **43:** 1022–3) and subsequent correspondence[1] prompts me to report another case of the use of propofol in a patient with porphyria.

A 31-year-old female was recently found to have hereditary coproporphyria. She presented for colposcopy, radical diathermy and possible cone biopsy of cervix. She stated that 20 out of 22 previous general anaesthetics and operative procedures were associated with acute exacerbations of what were subsequently recognised as symptoms of acute porphyria. These were usually in the form of abdominal pain, but on two occasions major neurological deficits had occurred. She carried a list (origin unknown) of 'Drugs unsafe in acute porphyria' which effectively eliminated all other local and general anaesthetic agents than propofol. She was completely asymptomatic at this time.

Propofol was used as the principal anaesthetic agent. Premedication was with intramuscular pethidine 75 mg; propofol was given in incremental doses to a total of 270 mg, while N_2O 60% in O_2 was administered via a facemask. The duration of the procedure was 20 minutes.

Anaesthesia was uneventful and the patient was awake and asymptomatic in the recovery room. She developed lower abdominal pain on return to the ward and requested analgesia. Pethidine was prescribed and this pain recurred at intervals over the next 3 days. A urine sample was obtained at induction and 12-hour collection commenced 12 hours later on the advice of our biochemist. The results are shown in the Table. The specimens were received by the laboratory on separate days and the laboratory procedures have been reviewed to exclude the possibility of handling error.

Table 1. Results of urinary porphyrin analysis.

	Before operation nmol/litre	After operation	Reference range
Porphyrin total	1333	522	0–300
Porphyrin/creatinine ratio	71.3	43.1	< 35
Uroporphyrin	146	120	0–40
Coproporphyrin	1080	365	0–180

The association between a single administration of propofol or any drug and a significant change in urinary porphyrin levels, either an increase as reported by Weir and Hodkinson or a decrease as in this case does not suggest a causal relationship either way. Any such suggestion must be highly guarded especially in association with surgery since there are so many other potent stimuli. This case also highlights the potential difficulty in the interpretation of symptoms in these chronically ill patients. However, the collection of urine specimens before and after operation, whenever possible, could help in the determination of the porphyrinogenicity of an anaesthetic agent in susceptible patients.

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The Model Malawi

We read Dr Fenton's article (*Anaesthesia* 1989; **44:** 498–503) with great interest but were surprised since Dr Fenton did not participate in the concept and design of the Malawi Anaesthetic Machine.

The firm Simonsen and Weel, the Danish International Development Agency (Danida), the Ministry of Foreign Affairs, Copenhagen, Denmark, the Head of the Danida Mission, Harare, Zimbabwe, and the Danida project

manager in Malawi, cooperated to publish some data and facts about the project.

Dr Fenton describes a mere 20% of the project. He refers to Ezi-Ashi's splendid article,[1] but omits to explain how the problems were solved.

The Danida project consists of many parts including the provision of 42 anaesthetic machines and 102 oxygen concentrators.[2] Stores (spares included), service centres (tools included), extensive training of technicians both in Denmark and locally and training of two anaesthetists in Denmark in a University Hospital and in the S & W factory were provided by Danida. Danida have guaranteed that they will continue to support the project in the future. S & W Medical Technology, UK, was not involved in the project; S & W Roskildevej 14, DK-2620 Albertslund, Denmark developed the equipment.

The pressure in the vaporizer is always atmospheric under normal conditions. Should the input flow exceed the patient's minute volume, the surplus gases pass through the positive pressure relief valve (PPRV) which is permanently open, if the pressure in the system increases to about 0.8 kPa. The safety valve also makes it impossible to give artificial ventilation by using the reservoir bag, since the result of a positive pressure in the inlet part of the vaporizer can cause an undesired higher outlet concentration. This will only work if the screws at the safety valve are *not* tightened.

If the supply of fresh gases through the Rotameter fails or if a subatmospheric pressure less than 0.03 kPa develops, the patient breathes room air through the underpressure valve.

We had anticipated some problems with the firm selling oxygen so Danida supplied all hospitals with reducing valves ('bull-nose') for oxygen and nitrous oxide and have ordered 120 emergency oxygen cylinders. These should now be in the country although they were not included in the original project. Some of the district hospitals now have extra oxygen concentrators, but all district hospitals were equipped with two in 1987.

Water can cause problems. All hospitals are instructed to drain daily and in the rainy season more frequently than twice a day. It is natural that they have to drain more frequently near the lake where relative humidity may be 97.5%. Water accumulates in the air systems: our new oxygen concentrator avoids this.

The use of repeated doses of suxamethonium before an adequate level of etherisation is achieved is strange and is surely not a technique for trainees. The problems with children[1] would not have happened had Dr Fenton not tightened the screws at the positive pressure relief valve.

The machine can be used in all the four modes described by Ezi-Ashi[1,2] and some other modes. The design of the anaesthetic apparatus Model Malawi makes it easy to use with a low pressure ventilator,[3] instead of manual ventilation, provided a pressure vaporizer is substituted. However, there is no oxygen concentrator which can supply oxygen at sufficient pressure for use with a high pressure ventilator.

The equipment was tested with a ventilator (Manley MPP 2000) but this part of the project was stopped because of unauthorised alterations of the anaesthetic equipment in the Southern region of Malawi. The oxygen concentrators are now in use with a Manley Pulmovent (MPP 2000 ventilator) at Dedza District Hospital.

Ether and halothane vaporizers were chosen because these two anaesthetic agents are most commonly available. A trichloroethylene vaporizer is not incorporated in the system, because the use of this agent is progressively decreasing. The Malawi Model can be used with nitrous oxide for special cases but nitrous oxide is usually too expensive for regular use.

It was agreed at a meeting held at 9 Bedford Square about oxygen concentrators in 1989 that an oxygen analyser should ideally be built into the system. A compromise suggestion was that a device should be designed which would indicate when the concentration decreased below 70%.

We have more than 15 years' experience with oxygen concentrators and we have never experienced a *sudden* decrease in concentration to 21%. It happens slowly over a period of one year, so all oxygen concentrators are monitored on a half-yearly basis.

The equipment is designed in accord with ISO codes and practices.

Any unauthorised modification of the equipment is not acceptable to the manufacturers: no responsibility for any complications which occur as a result will be accepted.

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A reply

Thank you for the opportunity to answer this letter: to those statements that require comment my reply is as follows.

The article does not claim to describe the entire Danida project; as stated, it is a report on the experience in one region.

A patient's minute volume is in practice often less than the fresh gas flow and the consequent patient system pressure of 0.8 kPa disturbs the normal function of the Ambu valve, especially when the paedivalve is used with tracheal intubation in small infants. A hole in the reservoir bag or substitution of the reservoir bag with an open-ended reservoir tube ensures that pressure is always atmospheric.

Emergency cylinders were not available during the study period.

Guidance on the best management in cases when strong patients who are half anaesthetised and whose lungs are ventilated with the maximum inspired concentration of ether but who are nevertheless at the same time trying to extubate themselves and climb off the table during surgery would be much appreciated!

The problem that occurred with the paedivalve was *before* any modifications were made.

Ezi-Ashi's article specifies that electricity can power a concentrator, which in turn can drive a ventilator, without and with nitrous oxide, respectively, 'providing all the facilities of modern inhalation anaesthesia'. This is not possible with the unmodified Malawi machine.

The incorporation of a facility to use nitrous oxide in a machine to be operated by relatively untrained paramedical

staff in a developing country is surprising. The purity of oxygen is variable and the machine was not tested in the field by an experienced anaesthetist.

The draft standard for the transoxycon states that the apparatus should not be capable of delivering less than 70% oxygen 'at the maximum design flow'. This is very different from what the authors state, as far as practice in developing countries is concerned, since an 'indication' that the percentage oxygen is falling is not an adequate safeguard.

'Rapid' was the word used: such a decrease in oxygen percentage that occurs when flow is increased could be termed 'rapid'.

The point about responsibility is noted. However it should be said that all the complications occurred before the modifications were made.

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Airway obstruction after tracheostomy

An 87-year-old woman presented for cataract extraction with intra-ocular lens implant under general anaesthesia. She was well and very active for her years. She denied any previous anaesthetic and complained of no cardiovascular or respiratory symptoms. Physical examination was normal.

No premedication was given. Anaesthesia was induced with thiopentone 225 mg through an indwelling cannula. Her trachea was easily intubated with a size 8.0 mm cuffed oral tube cut to 22 cm after suxamethonium 50 mg and manual ventilation of her lungs through a mask and airway. She was transferred to the operating theatre where anaesthesia was maintained with oxygen and nitrous oxide supplemented by isoflurane via a circle absorber. Ventilation was by hand, but as respiratory efforts soon returned, she was allowed to breathe spontaneously.

However, it was immediately obvious that her airway was obstructed. The tracheal tube was checked, found to be unkinked, correctly positioned, and the cuff was deflated but the airway obstruction persisted. The tube was changed for a size 8.0 mm cut to 20 cm. The original tube was checked and found to have a patent lumen with no cuff herniation. The obstruction remained with the new tube but on extension of the neck, with the chin supported, the obstruction was completely relieved. The operation proceeded satisfactorily to its conclusion with the head in this position and there were no changes in tidal volume or end-tidal carbon dioxide measurements.

A fine-bore suction catheter was passed down the lumen of the tracheal tube when surgery was completed. An obstruction was encountered at 20 cm with the head in the extended position. Oxygen 100% was administered, she was extubated without incident and breathed satisfactorily with a Guedel airway in place. She recovered consciousness within a few minutes.

A close examination of her neck then revealed an almost invisible tracheostomy scar. The patient admitted on close questioning to a history of diphtheria in 1911 and an emergency tracheostomy.

It was assumed that a previously asymptomatic tracheal web or narrowing had occluded the distal end of the tracheal tube. Chest and thoracic inlet X rays performed subsequently confirmed a tracheal narrowing at the level of C_6 vertebra. Distal to the stenosis the trachea was deviated to the left.

This incident illustrates two important points: physical examination may disclose potential problems not revealed by the history, and a correctly placed tracheal tube does not guarantee an unobstructed airway.

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Failure of a valve in a Bain system: a dangerous design?

Sudden failure of an anaesthetic system for manual control of ventilation during induction of anaesthesia may have serious consequences.

A patient was pre-oxygenated with 100% oxygen delivered through a Bain system. Anaesthesia was induced with thiopentone and the patient paralysed with vecuronium. The valve of the Bain system (Cory Bros 002/BEV) was then partially closed and manual control of ventilation was attempted. This was unsuccessful, even when the valve was fully closed. It became apparent that there was a persistent fresh gas leak through the valve when the bag was squeezed. Immediately a self-inflating resuscitation bag was used to inflate the lungs and the Bain system was changed for another with a competent valve. The rest of the anaesthetic progressed uneventfully. The faulty valve was checked before commencement of the list and found to be competent. The same valve was used during manual inflation of the lungs in three patients before its failure.

The reason for the failure was apparent on close inspection of the valve (Figs 1–3). The new design of this particular valve consists of a valve control (A) and a lock nut (B) with an outer thread. The shaft of the valve control passes freely through the centre of the lock nut then has a larger diameter lower part (C) with the same size outer thread as the lock nut. Both these thread into the valve casing which is surrounded by a gas-tight swivel scavenging mount (D). The lock nut is screwed tightly into the valve casing and the valve control can move through 360 degrees under normal conditions. However, the lock nut may become loose. This results in the lock nut being unscrewed with the valve control when the valve is open (Fig. 1). This should be suspected if the valve control rotates further than 360 degrees. The valve will still function when the valve control is closed as long as the lock nut threads are in contact with the valve control threads or the two sets of threads are in line. If the lock nut becomes free from the casing and the two sets of threads are not in contact and off line (Fig. 2), the lock nut threads become crossed with the casing threads when the valve control is screwed down. The valve appears to be shut but the valve control is held clear of the valve by the jammed lock nut (Fig. 3). The valve is still open and manual inflation of the lungs becomes impossible. This was

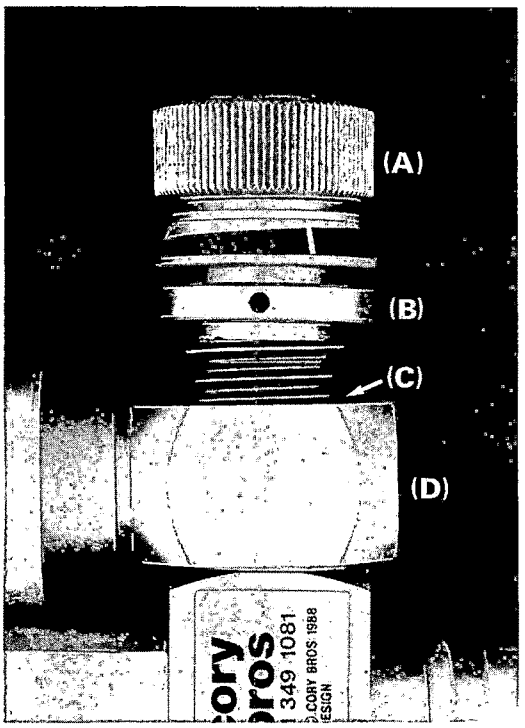

Fig. 1. Valve control unscrewed from valve casing with lock nut. (A) Valve control; (B) Lock nut; (C) Lower threaded end of valve control; (D) Valve casing surrounded by a gas tight swivel scavenging mount.

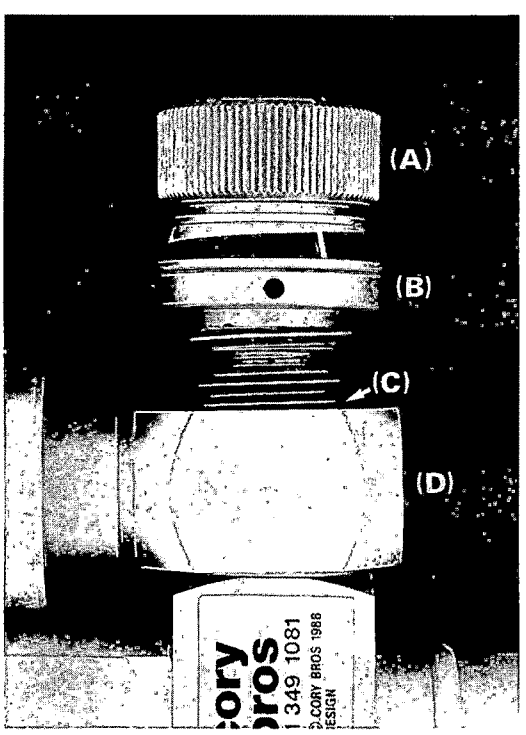

Fig. 2. Lock nut threads are not in contact and off-line with valve control threads.

the case in the above incident. Such cross threading may also cause permanent damage to the lock nut or casing threads.

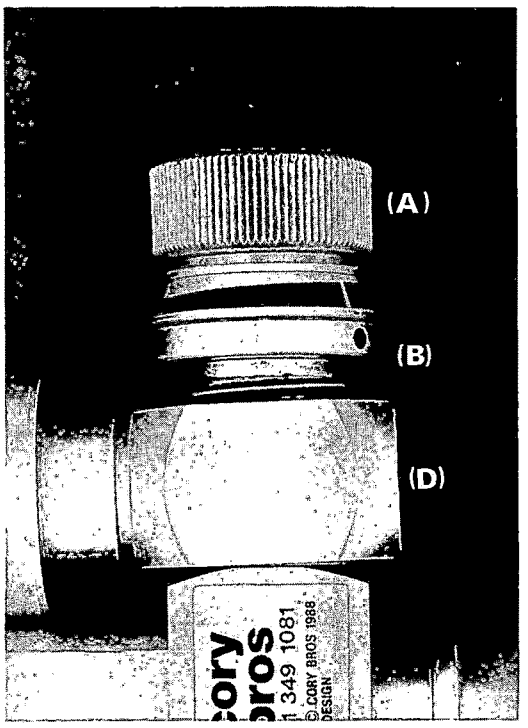

Fig. 3. Cross-threaded lock nut holds valve control clear of valve.

A check of this type of valve must include inspection of the lock nut to ensure that it is properly engaged in the casing. However, if the lock nut is loose it may only be screwed down with the fingers since it is completely circular. This is in contrast to the older model of this valve which could be tightened with a spanner. This hospital has now withdrawn all such valves from service.

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A reply

The manufacturing and assembly process which includes the tightening of the collar referred to by Dr Breen, was modified and improved in July 1989 and we are satisfied that, under normal conditions of use, this situation will not occur. However, it would appear that the collars on a very few valves, manufactured just before this modification, may not have been fully tightened and were not detected by our Quality Control.

We agree with Dr Breen that valves should be routinely checked before use to ensure they are functioning correctly. Should there be any doubt about the integrity of the collar, we will be pleased to carry out an inspection, free of charge.

The 002BEV Bain Valve is precision engineered to allow correct response using finger tip rotation of the control knob. It is clearly stated, in the instruction leaflet which accompanies each one, that when opening and closing the valve a definite 'stop' will be felt at its maximum positions. The control knob should *not* be forced past these positions.

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Visible expiratory valves

It is evident from Sansome and Bacon's response (*Anaesthesia* 1989; **44:** 1006) to my description of a hybrid expiratory valve, which incorporates the best features of three other valves, that they have failed to grasp the clinical advantages of my valve. Their statement, that the modification of a Medishield valve allows obstruction of the airway to be differentiated from a failure to obtain a seal, whereas use of the hybrid valve does not allow this distinction to be made, is not true. Indeed the *raison d'etre* for the composite valve is to allow just such a distinction to be made at a glance. This is possible because every aspect of the valve's function is clearly visible from all sides and the anaesthetist's direct view of the valve stem is magnified.

Thus in respiratory obstruction the valve disc can be seen to lift from its seat and to hover stationary in the gas stream. Failure to form a seal at the mask on the patient's face will prevent the stationary valve from lifting at all. Both of these conditions need to be differentiated from: apnoea due to whatever cause, mouth breathing in dentistry and from rarer events which may cause the valve disc to remain on its seat; for example, obstruction of the scavenging hose or failure of the gas supply. It is up to the anaesthetist, and not the valve, to make the distinction.

Protrusion of the valve stem in the modification described by Drs Bacon and Sansome introduces a potential hazard: any inadvertent contact with the top of the valve by the theatre drapes may stop the valve from functioning. A manufactured version would have to incorporate some sort of guard to prevent this from happening, as in the Ruben valve. The hybrid valve is totally enclosed and is not vulnerable in this respect.

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The Finapres and collateral circulation in the hand.

We read with interest the article of Drs Glavin and Jones (*Anaesthesia* 1989; **44:** 594–5) on the assessment of collateral circulation of the hand with the Allen's test, Doppler ultrasound, pulse monitor and pulse oximeter. However, none of these methods was fully reliable. It is probable that a systolic blood pressure in the fingers of less than 40 mmHg indicates an inadequate circulation.[1] A new noninvasive monitor, the Finapres, provides direct, instant measurement of the blood pressure in the fingers.[2] It records the pulse wave and the systolic, mean and diastolic blood pressures from any of the fingers and thereby gives a qualitative and a quantitative assessment of the blood pressure to the finger.

It is possible that the use of this monitor may allow accurate assessments of the state of the hand circulation. We have used it to assess the collateral circulation of five subjects with no abnormalities of their blood supply to the hand and five subjects who had undergone radial artery cannulation within the last 6 months. They all received a modified Allen's test; all made a fist and both ulnar and radial arteries were occluded for 30 seconds, the hand was extended and the ulnar artery pressure then released and the time to blush observed. The index finger blood pressure was recorded both before the test and after release of the ulnar artery by the Finapres. A similar test was repeated using the ring finger.

All subjects had a rapid flush after release of the ulnar artery and indicated a satisfactory collateral circulation. There was a decrease in systolic, mean and diastolic pressure for both groups though this was much greater in those subjects who had been previously cannulated (Table 1). This confirms earlier work which demonstrated thrombosis formation after arterial cannulation.[3] None of normal subjects had a systolic pressure in the thumb of less than 40 mmHg, although two in the previously cannulated group did; this was not detected with the Allen's test. There was little difference in the measurements between the ring and index fingers.

This small trial indicates that the Finapres may be a valuable aid in the assessment of the collateral circulation of the hand for arterial cannulation. It may also be useful as a method to detect the degree of radial artery occlusion that can occur after cannulation.

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Table 1. Mean (SD) percentage decrease in systolic, mean and diastolic pressure at the index and ring finger from the pre-occlusive values to those after ulnar artery release.

Finapres mmHg	Index			Ring		
	Systolic	Mean	Diastolic	Systolic	Mean	Diastolic
Cannulated	57 (25)	39 (43)	42 (41)	40 (19)	34 (23)	40 (27)
Normal	15 (10)	19 (11)	24 (11)	16 (8)	18 (10)	22 (6)

Tracheal placement of a gum elastic bougie using the laryngeal mask airway

Our experience of difficult intubation aided by the placement of a gum elastic bougie through a laryngeal mask airway (LMA) is similar to that described by Chadd *et al.*[1] This has led us to study the practice of this technique.

We achieved satisfactory first time placement of the LMA in 22 of 25 paralysed patients in a prospective series, confirmed under fibreoptic vision (through the lumen of the LMA). This success rate is similar to that published by

Payne.[2] We were then able to pass a gum elastic bougie into the trachea, under fibreoptic vision, in all cases where the LMA was in a good position. Passage of the bougie was made easier if its angulated end was made to point anteriorly followed by rotation through 180° as it cleared the aperture of the LMA, to bring the angulated end in line with the long axis of the trachea. This observation has prompted us to mark the bougie indicating both the direction of the angulated end and the point at which it clears the aperture of the LMA.

Blind tracheal placement of the modified bougie through the LMA (in the manner described) was successful in 21 of 25 patients in another series. All failures were associated with poor LMA position (again, confirmed under fibreoptic vision).

We agree with the suggestion[1] that the technique could be practised on anaesthetised patients in anticipation of the difficult case. Furthermore, we have found that this refined technique will result in correct tracheal placement of a bougie in the majority of cases, with or without the aid of a fibreoptic laryngoscope, provided the LMA is well placed.

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Tube placement after difficult intubation

An otherwise fit man aged 53 years was due to undergo excision of a tumour of the glomus jugulare. He had previously been noted to be a grade 3 difficult intubation[1] after anaesthesia for angiography of the tumour. He had been intubated on this occasion with an 8.5-mm Mallinckrodt 'Lo-Pro' tracheal tube, railroaded over a gum elastic bougie, with the aid of cricoid pressure.

It is our practice to cut the tracheal tube to a longer length than normally required when we are faced with an anticipated difficult intubation. This avoids the frustration of finding the tube to be too short when it is in the trachea. An 8.5-mm 'Lo-Pro' tube was therefore cut to 27 cm, but was secured firmly with the 24-cm mark at the incisors. Intubation was performed in the same manner as previously described. Routine checking of satisfactory tube placement consists of visualisation of the larynx when passing the tracheal tube, auscultation of equal breath sounds on both sides of the chest and an equal movement on inspiration of both sides of the chest wall. Other measurements and observations may be made to confirm placement: oxyhaemoglobin saturation (Spo_2), end-tidal carbon dioxide, the ease with which a gas tight seal may be made with inflation of the cuff, and more recently an oesophageal detector device.[2]

A combination of these tests confirms correct placement in the majority of patients, but it is prudent to carry out further investigation into the precise position of the tracheal tube after a difficult intubation and after positioning of the patient for surgery, if at all possible.

Despite many of the above observations being satisfactory in our patient, it became apparent that the tip of the tracheal tube was lying too near to the carina. The cuff (which had previously been observed to be of a normal profile) had expanded enough partially to occlude the bronchial tree after nearly one hour of surgery; this caused an increase in airway inflation pressure and a decrease in Spo_2. A direct visual check on the tube was not possible because of the nature of the surgery being performed, nor was it possible to aspirate the oropharynx, deflate the cuff and reinflate it to a suitable volume again. On this occasion increasing the Fio_2 to 0.5 coupled with gentle traction on the tube from under the towels proved adequate to reverse the decrease in Spo_2, and arterial blood gas showed adequate oxygenation. The profile of the cuff after extubation suggested that the left main bronchus had been occluded by expansion, as a result of the inward diffusion of nitrous oxide, and formed a neat herniation into the bronchus. This tendency of profile cuff tubes to conform to their environment makes it essential to know exactly where the tip of the tracheal tube lies in relation to the carina. This may be achieved by chest X ray with the neck in flexion and extension or by direct visualisation of the carina through a fibreoptic bronchoscope or laryngoscope.

Other aids to minimise the risk of cuff expansion would be to monitor the cuff pressure or to use a tracheal tube of the Lanz or Brandt types (Mallinckrodt) which have a dual pilot cuff, the inner one of which expands as nitrous oxide diffuses into the cuff. An alternative is to inflate the cuff with the gas composition to be used during anaesthesia.[3]

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Teaching fibreoptic nasotracheal intubation

We would like to suggest a useful hint. We have found that the novice may waste a considerable time by failure to realise the depth at which the tip of the endoscope is placed. The vocal cords come into view at or slightly beyond 15 cm from the anterior nares if the fibrescope is kept in the midline. The presence of a tracheal tube poised for 'rail-roading' prevents depth measurement from the eye-piece end. If the novitiate holds the distal end at the 15-cm distance this improves orientation. It is to be hoped that future designs of fibrescopes will have easily identifiable depth markers.

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Prolonged motor weakness after femoral nerve block with bupivacaine 0.5%

Prolonged sensory and motor block are described to follow single-shot nerve blocks in the inguinal region,[1,2] including femoral nerve block.[3] This phenomenon is however rarely reported after femoral nerve block with a catheter technique.

A 68-kg, 43-year-old female patient was treated for limitation of movement in the knee joint after anterior cruciate ligament repair 12 weeks earlier. An 18-G Teflon catheter was inserted 15 cm into the fascial sheath of the femoral nerve using a Seldinger technique. A nerve stimulator was used to aid placement which was uneventful. No parasthesiae were elicited and no vessel puncture was observed. The catheter was protected with a bacterial filter and 30 ml of bupivacaine 0.5% was injected. A complete femoral nerve block developed about 20 minutes later and block of the obturator nerve and the lateral cutaneous nerve of the thigh was also noted. The motor block, with inability to extend the knee, lasted for over 36 hours. There were still signs of sensory loss on the thigh and calf at 60 hours, which was discomfiting for the patient and the attending staff alike.

Possible explanations for prolonged motor block include intraneural injection of local anaesthetic, trauma to the nerve from a needle or external compression of the femoral nerve from a haematoma after inadvertent puncture of the femoral artery. However, neither seems likely in this case since the patient was awake and experienced no paraesthesiae or pain on injection. It remains to reassure the patient (and oneself!) that although distressing, this condition is self-limiting and a return to normal can be expected in 2–3 days.

Other authors have reported favourably on the use of a catheter technique using bupivacaine for 3-in-1 block,[4,5] but no mention of an abnormally long duration of action of bupivacaine was made nor in a further series of 104 patients.[6] Thus, this prolonged duration of action of bupivacaine would seem to be rare, nonharmful and self-limiting and does not detract from the usefulness of this technique.

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Dilution of propofol

Propofol is used as the induction agent in an increasing proportion of children for procedures such as lumbar puncture, bone marrow aspiration and CT scanning, where the rapid recovery characteristics of propofol are ideal.

The majority of children have Hickman central venous catheters in place for the administration of chemotherapy, antibiotics, blood products and to avoid repeated venepuncture. It was noticed when anaesthesia was induced with propofol via the Hickman line, that the incidence and severity of excitatory phenomena was considerably higher than the reported series (20–30%)[1–3] and was more marked the younger the child. These reactions included coughing, crying, laryngospasm and involuntary movements. A number of children actively refused to have the 'white' injection via the Hickman line on subsequent occasions, which was puzzling since there was no apparent pain on induction.

It seemed likely that these observations were related to the fact that the dose of propofol was given directly into a central vein, and since the deadspace of the line is approximately 1 ml and the volume of propofol as little as 2.5 ml in a 10-kg baby, a relatively large bolus reaches the brain very quickly.

It was difficult with the small volumes involved to give the dose slowly, so it was decided to dilute the propofol in equal parts with saline. We found the quality of induction much improved with the diluted mixture; 20 patients received a mean dose of 2.7 mg/kg at an average rate of 1.3 mg/second. Side effects were seen in only two children: one exhibited mild distress and another had hiccoughs and some rigidity after induction. Children who had refused propofol in the past accepted and had no complaints about the 'new' induction agent.

This improvement is almost certainly as a result of the decrease in size and speed of the propofol bolus which reaches the brain. We consider that dilution of propofol is a simple means whereby a smoother induction can be achieved in these cases.

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Problems associated with limb tourniquet deflation

The explanation for the significant decrease in cerebral pressure as a consequence of using a lower limb tourniquet described by Eldridge and Williams (*Anaesthesia* 1989; **44:** 973–4) is, as they state, predictable. The transient increase in end-tidal CO_2 and decrease in blood pressure is in my experience especially noticeable during total knee replacement.

Dickson *et al.*[1] demonstrated a significant increase in end-tidal CO_2 levels after the release of an extremity tourniquet. This was threefold higher in patients with surgery of the lower extremity (0.67 to 2.4 kPa) when compared to the upper extremity (0.13 to 1.6 kPa). They, too, recommend the benefit of end-tidal CO_2 monitoring and hyperventilation just before tourniquet release, especially in patients with raised intracranial pressure.

These changes may be attenuated by several deflations and inflations of the tourniquet before it is removed at the end of surgery. This might benefit the patient at risk.

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Ketamine and video nasties

Ketamine is advocated as a suitable anaesthetic for short procedures, particularly in children. One of the major disadvantages of ketamine in adults is emergence hallucinations which can leave the patient distressed and bewildered. Hallucinations are said not to occur in children.

A 40-kg 10-year-old boy with severe pain from a pelvic Ewing's sarcoma underwent urgent radiotherapy as a palliative measure. Epidural opiates were giving limited pain relief. Anaesthesia was induced intravenously after 0.2 mg glycopyrronium with 80 mg ketamine. Supplementary doses of ketamine were given over the subsequent 10 minutes. The child received a total dose of 150 mg. Diazemuls 2.5 mg was given intravenously shortly before the procedure finished.

The child said that there was a green monster climbing up his bed on recovery. He identified the monster by name. His mother who was present throughout remarked that he was describing a character from a horror video they had at home; a video which the child should not have seen. The hallucination fortunately lasted only 3 minutes and the child appeared calm thereafter.

The question arises, are children who watch home videos with a science fiction or horror theme more likely to have emergence hallucinations after ketamine? Maybe our pre-anaesthetic assessment should extend to the child's illicit viewing habits!

Newcastle General Hospital, Newcastle-upon-Tyne NE4 6BE I.H. SHAW S.P. MOFFETT

A disposable device for patient-controlled analgesia with fentanyl

The disposable device for patient-controlled analgesia (PCA) described by Drs Rowbotham, Wyld and Nimmo (*Anaesthesia* 1989; **44:** 922–4) expands the range of PCA devices. There is obviously no initial capital cost for the device, but there is a revenue cost, and the authors give no estimate of this. They are not justified in their implication that it is a cheaper alternative to existing electronic systems.

Monitoring of the patient is an essential part of care during the use of PCA. Accurate data collected about the total quantity of opiate administered, number of boluses and attempts has often proved useful if postoperative problems occur. The lack of easy access to such information is a possible drawback of this system.

James Paget Hospital, Great Yarmouth NR31 6LA W. NOTCUTT

General anaesthesia in the presence of a spouse

The problem of the husband who insists on being present at his wife's general anaesthetic for Caesarean section (*Anaesthesia* 1989; **44:** 618) is one that obstetric anaesthetists will face with increasing frequency in the future. Indeed, on a recent television discussion programme, it was confidently stated (not by an obstetrician or anaesthetist) that the husband's right in this respect was absolute, and that refusal to comply with his demands should lead to immediate transfer of the care of the patient to a more sympathetic obstetrician (a difficult task in the event of severe fetal distress!).

The husband's presence during general anaesthesia does not benefit either of my patients, in contrast to the situation when a regional block is used, and so I have tended automatically to refuse these requests. However, as was pointed out on the same programme, mothers who have operative delivery under general anaesthesia sometimes believe that the baby presented to them afterwards is not really theirs; this may cause considerable distress in the post-partum period and, in the most extreme cases, interfere irrevocably with the bonding process. This can be alleviated by the husband, if present, acting as a 'family witness' of the birth. If this is indeed the case, the presence of the husband may benefit *both* patients, and my routine response no longer applies. If, in the future, these concerns were voiced by prospective parents, one would be obliged to consider the request very seriously.

Dr Russell (*Anaesthesia* 1989; **44:** 932–3) suggests that we should be prepared to perform induction and intubation with the spouse breathing down our necks, and argues in

mitigation of his view that our obstetric colleagues are prepared to operate in the husband's presence. The circumstances are hardly comparable, and most surgeons would certainly baulk if the partner were intently watching their every cut, rather than holding a hand and stroking a brow behind a well-sited screen.

Should this situation arise in the future, my duty will be fulfilled by having the husband come in after the proceedings are underway, to witness the birth; then he will be shepherded out with the baby.

City Hospital,
Nottingham NG5 1PB

D.G. BOGOD

'Permission' to publish

We were interested to read the report by Drs Stuart-Taylor and Crosse (*Anaesthesia* 1989; **44:** 916–7) but why did they consider it was necessary to ask permission from the surgeon in order to publish their report? The case arose as a problem during anaesthesia and was dealt with by anaesthetists who are professionally qualified in that specialty. They were presumably not acting as technicians under the direct control and responsibility of the surgeon but as independent professionals working alongside a surgeon. Did they ask permission from the surgeon to treat the medical complications arising during anaesthesia and surgery? Do surgeons ask our permission to publish reports of interesting cases?

This report is of course only one of many to add such acknowledgments following a long tradition. We all wish to work in close cooperation with our surgical colleagues but the days should have passed when anaesthesia was regarded as an unskilled job which was delegated by the surgeon to any willing pair of hands and for which the surgeon took responsibility. After nearly 150 years as a specialty with a sound academic and scientific basis it is time that anaesthetists accepted the professional role of their own specialty. There is little point in forming a College of Anaesthetists if we do not even recognise ourselves.

Frenchay Hospital,
Bristol BS16 1LE

S.W. CONIAM
A.W. DIAMOND

A reply

Thank you for the opportunity to respond to Dr Coniam and Dr Diamond. When we wrote the case report we considered every possible clinical and pharmacological criticism that we might receive, but it did not occur to us that we might be criticised for a traditional medical courtesy.

Members of our specialty should never feel subservient or threatened by colleagues in other specialties. The existence of a College of Anaesthetists is irrelevant, 'changing the packaging does not alter the contents'. It is our tradition of skill, knowledge and total professionalism which has earned us respect, and anyone truly worthy of respect need neither demand respect, nor fear losing it by minor courtesy.

To set the matter straight we wrote the case report and, out of courtesy to a colleague and friend from Medical School days, informed the surgeon.

In a lighter mood, bearing in mind that the opportunity to write the case report on this unexpected pharmacological problem was brought about by the surgical team's failure to follow our instructions (see paragraph 3—a plea for noradrenaline), it did seem that they deserved some recognition!

Southampton General Hospital,
Southampton SO9 4XY

M. STUART-TAYLOR
M. M. CROSSE

Anaesthesia, 1990, Volume 45, page 424

Safety Action Bulletin

Portable Respirable Air Compressors: risk of air supply failure (SAB) 90 (1)

A portable compressor, which supplied air to an oxygen air blender and was connected to a neonatal ventilator, failed in use. 100% oxygen was therefore delivered to the baby. Systems like this should be used with an oxygen monitor and alarm.

Fresenus Injectomat Syringe Pump Models 30, 50S: misalignment of control knobs (SAB) 90 (5)

Over-infusion incidents were caused because of misalignment of some control knobs with their scale markings on these pumps. The alignment should be checked and appropriate action taken to correct any discrepancy.

Erratum

Anaesthesia, 1990, Volume 45, pages 49–52

Goldenhar's syndrome: an analysis of anaesthetic management

A retrospective study of seventeen cases

R. Madan, A. Trikha, R. K. Venkataraman, R. Batra, P. Kalia

A printer's error has resulted in the omission of a line of text in the last paragraph of the first column of this paper. The first two sentences of this paragraph should read:

> Surgical techniques ranged from lamellar keratoplasty, tarsorrhaphy, needling and syringing, and dermoid excision, to examination under anaesthesia. All patients were premedicated with intramuscular atropine 0.01 mg/kg one hour before induction.

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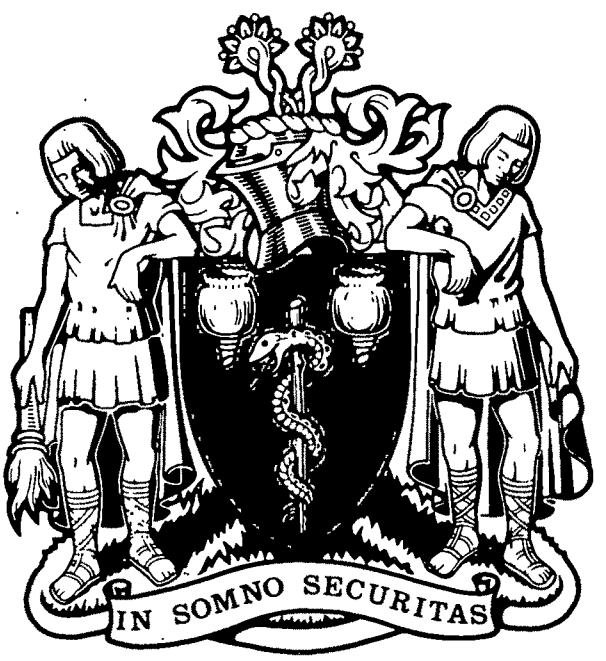

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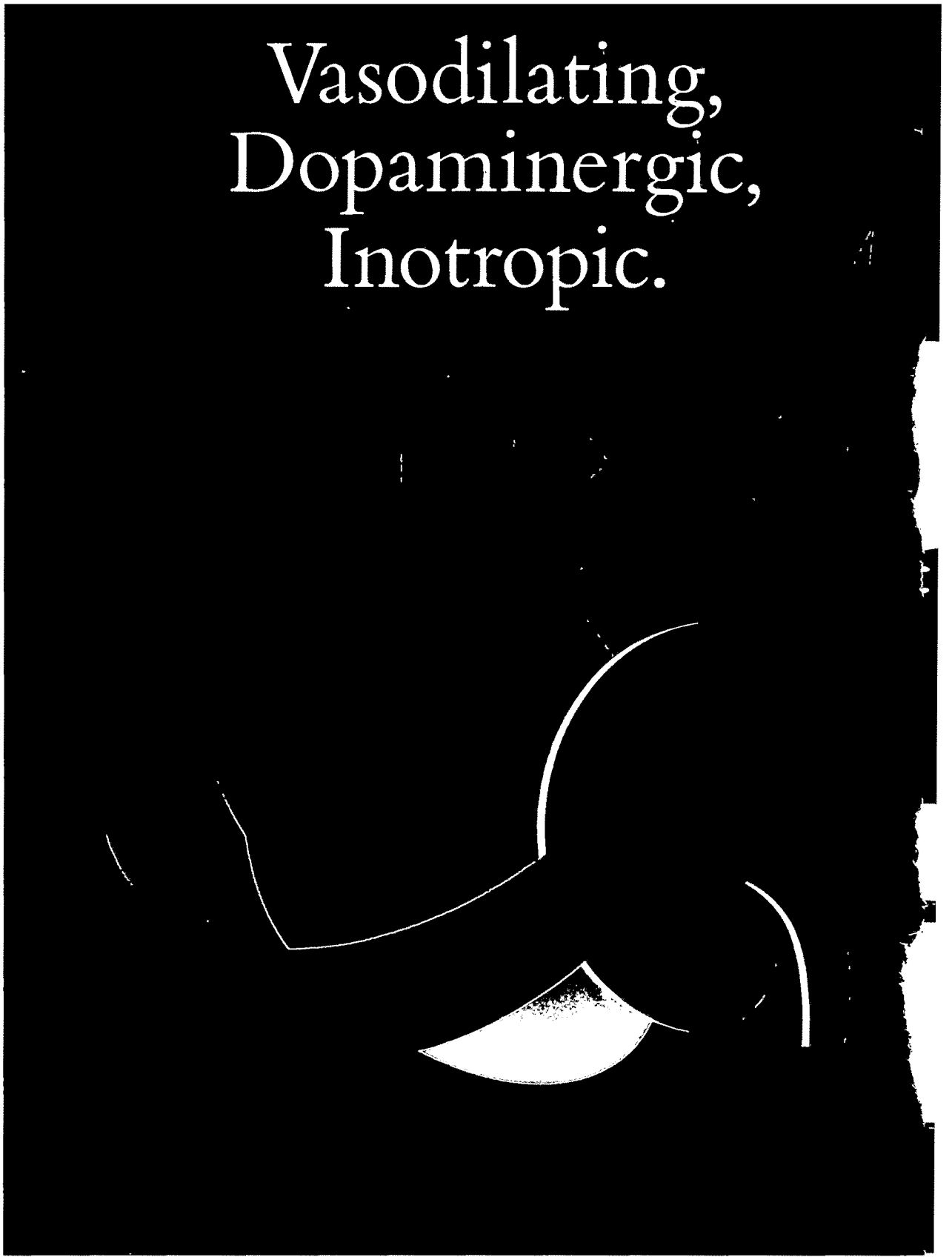

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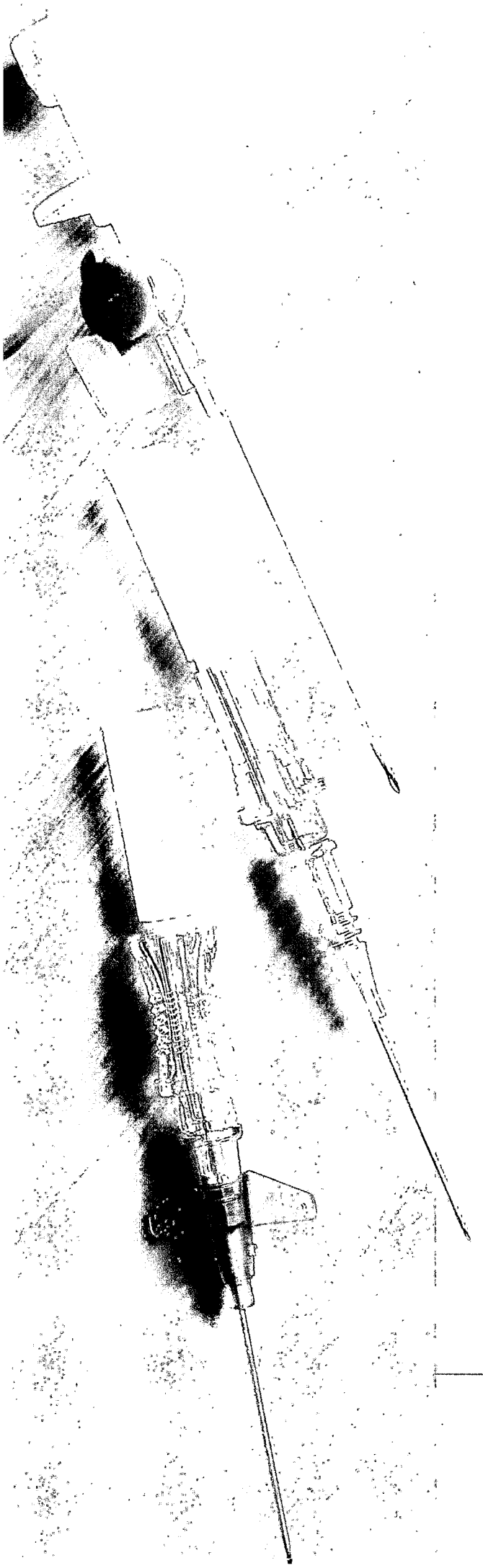

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Anaesthesia, 1990, Volume 45, pages 425–426

Editorial

Checklists and patient safety

Most anaesthetists ensure there has been some check of an anaesthetic machines before its use.[1] This procedure may entail the use of a formal checklist, or it may be a more rudimentary version of the 'kick the tyres, slam the doors, turn the lights on and off' kind. The latter method is akin to a pilot throwing his leather jacket over the back of the seat with merry cries of 'chocks away'; then off into the wide blue yonder, and it is only a matter of time before a 'wizard prang' occurs!

Those of us used to the relatively unsophisticated anaesthetic machines of the 60s and 70s may make basic mistakes when confronted with one of the 'mighty Wurlitzer' variety that are becoming more common. Checklists have been available for some time and yet there is ample evidence to suggest that their application is by no means universal,[2] despite the fact that many lists were introduced after a serious accident with an anaesthetic machine.[3] The argument follows from this that it is both reasonable and prudent to introduce mandatory checklists as an aid to patient safety.

The United States of America is in the forefront of the introduction of mandatory checklists. The Food and Drug Administration introduced anaesthesia apparatus checkout recommendations in August 1986. The preamble states 'this checkout, or a reasonable equivalent, should be conducted before anesthesia. This is a guideline which users are encouraged to modify to accommodate differences in equipment design and variations in local clinical practice. Such local modifications should have appropriate peer review'.[4] Recommendations from a federal body that contain the word 'should' are not voluntary; they are mandatory.

An Association of Anaesthetists of Great Britain and Ireland Working Party has considered the matter of checklists.[5] The Working Party does not suggest that checklists be mandatory as they are in other countries like the USA, Australia and Germany. The Association does not work by prescription, but responds to the demands and needs of its members. The Association has responded in this instance, by obtaining the best advice and passing it on to the membership to do as it pleases. Nevertheless, an 'Association view' is clearly stated. The report recommends that anaesthetic machine check procedures *should* be performed at the beginning of each operating theatre session.

The anaesthetic machine is a key component of safety, and more and more machines will have automatic monitors built into them to provide added vigilance over both machine and patient. System oxygen concentration and exhaled patient volume monitors may provide early warning of hypoxic mixtures, system leaks or accidental disconnexions. Integration of these and other monitors (capnometry, pulse oximetry, noninvasive blood pressure) into the anaesthesia system helps to ensure that monitors are switched on and functional before activation of gas delivery and improves the management of the multiple machine and patient connexions.[6]

The argument has been advanced that a simple check at the beginning of anaesthesia is sufficient, and that any faults will be picked up and dealt with intra-operatively. This may be true in the majority of cases, but modern anaesthetic machines are both large and complex: they need to be checked carefully to avoid potential problems. It is just as important to check the older, simpler machines as they approach the end of their working lives. Many hospitals may have found it difficult to replace older machines because of restraints placed upon their equipment budgets.

The anaesthetic machine checking procedure recommended by the Working Party is simple, and should ensure high compliance. It is not intended to replace schemes devised by individual manufacturers for their machines. The belief of the Working Party is that the introduction of a checklist based on the use of an oxygen analyser will mean safer practice. This piece of equipment therefore, will become standard. It is pleasant to speculate on the prospect of managers dashing round to anaesthetic departments to offer extra money for such equipment, having been won over by the argument that anything that will increase patient safety and reduce the possibility of litigation and thus cost, is a worthwhile use of their hard-won resources.

Performance of such checks forms part of our working day and should not be viewed as an additional burden. However, the concept of making a pre-anaesthetic machine check *compulsory* is both controversial and provocative. There will be arguments that checks are already carried out by qualified personnel such as anaesthetic nurses, operating department assistants (ODAs), and that for the anaesthetist to repeat them would be a time-consuming reduplication of effort.

The question of who should carry out the checks has already been raised by members who have tried out the proposed checklist after it was circulated for comment. There is no doubt in the writer's mind that the anaesthetist must check the anaesthetic machine before a theatre session, since ultimate responsibility lies with the anaesthetist and cannot be delegated or denied. This does not mean that the anaesthetist should carry out every part of the check personally. It is probably sufficient for the check to be carried out by the anaesthetist with another appropriately trained person who could be a nurse or ODA, rather as pilot and copilot check before take-off. This suggestion has the additional advantage that the time taken to perform the check would be reduced.

The report also suggests that a written record of the check be kept in either a specific logbook or on the patient's anaesthesia record. Is this necessary? A simple test of negligence is whether or not the anaesthetist has maintained a reasonable standard of care in treating the patient. A standard of care is, in general, determined by review of written records and the importance of good record keeping is emphasised every year by the defence organisations in their annual reports. Records made today may have to be defended many years from now.

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A general rule says 'if it isn't written down, it wasn't done'. Keeping a written record of check procedures makes sense.[7]

There may be other potential benefits. Anaesthetists in the United States have found that their malpractice insurance can be reduced by declarations that they have adopted and abide by checklist procedures and minimal monitoring standards. They are paying the same rates as general practitioners in some states.[8] This may be an idea that could be taken to our defence organisations.

It is recognised that it may not be possible to carry out a full check in an emergency situation. This should not be a problem where there is a dedicated emergency theatre since it should have been possible to check the machine at an earlier time. Should a true emergency occur it is unreasonable to insist that a full check be carried out, but it would seem reasonable to document the circumstances when time permits.

The recommendations for standards of monitoring published by the Association in July 1988 were 'somewhat watered-down before publication because some members of Council had strongly objected to too many words such as 'must''.[9] Times change, and by the College of Anaesthetists' symposium in November of that year the recommendations were thought to be in need of strengthening.[9] The current mood seems to favour the adoption of higher standards of safety and patient care. The use of checking procedures seems an excellent way to achieve these objectives.

Recent articles have suggested that the introduction of checklists may be a potent factor in reducing both the number and frequency of critical incidents during anaesthesia,[10] and that use of checklists and adequate monitoring with current technology may avoid up to 50% of patient injuries: this makes these procedures cost effective in injury prevention.[11] However, we should never forget that one of the many corollaries to Murphy's Law applies; 'it is impossible to make anything foolproof because fools are so ingenious'.[12]

J.E. CHARLTON

Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA

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Editorial notices

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979: **1:** 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia, 1990, Volume 45, pages 427–435

Pre-induction behaviour of children

A review of placebo-controlled trials of sedatives

J. O. MORGAN-HUGHES AND J. A. BANGHAM

Summary

Placebo-controlled trials of sedative premedication in children are reviewed in an attempt to determine which drugs have been shown to reduce the frequency with which children cry or appear apprehensive. Small samples and inappropriate statistical methods limit the value of many of the studies. Most of the drugs tested will, in sufficient dose, increase the proportion of children who are asleep. Only intramuscular opioid analgesics, either alone or in combination with other drugs, have been shown repeatedly to increase the frequency of calm behaviour in those who are awake. There is some evidence, however, that intramuscular placebo controls have a lower frequency of calm behaviour than oral placebo controls.

Key words

Anaesthesia; paediatric.
Premedication; antisialagogues, benzodiazepines, barbiturates, phenothiazines, opioids.

Calm behaviour of children in the anaesthetic room is a worthy objective for the anaesthetist. Psychological effects of anaesthesia in children have been reviewed recently.[1] Disturbed behaviour during induction of anaesthesia may be associated with arterial oxygen desaturation.[2]

The intention of this review is to establish which premedicant drugs have been shown to reduce the frequency with which children appear apprehensive, cry or struggle at induction of anaesthesia in comparison with unsedated control patients.

Methods

A Medline Search was made using the key words: *premedication* or *preanaesthetic medication* with *infant, preschool child* or *child*. The search included the period from the establishment of the Medline database in 1966 to December 1988. Earlier references were obtained from the bibliographies of the papers found by the computer search.

It is important in any discussion of the effect of premedicant drugs given in conjunction with anticholinergics to establish what constitutes a suitable control. Hyoscine and atropine have been compared in clinical trials. Eger *et al.*[3] studied the behaviour of children premedicated with barbiturates and opioids with atropine or hyoscine, and found that significantly more children were drowsy and fewer were fretful after hyoscine than after atropine. The behaviour of children premedicated with hyoscine has been compared to that after premedication with atropine when these drugs were given with morphine,[4] diazepam[5] and trichlofos.[6] On balance, hyoscine appears to have a sedative effect on children which is evident when it is used in combination with some other drugs. Its lack of current popularity may be attributed to less reliable absorption following oral administration, occasional confusion, excessive antisialagogue effects and less reliable effect on heart rate than atropine.[7] However, for the purpose of this review, children who had been given atropine alone were considered to be unsedated. In addition, children given hyoscine alone were considered to be unsedated controls, provided that the sedated children with whom they were compared were given the same anticholinergic premedication by the same route.

The search revealed 30 reports of 29 trials of sedative premedication in children, in which an unsedated control group was included.[3,4,8–35] The drugs tested by the various authors are shown in Table 1.

Most studies categorise children as, for example, calm, restless, crying, or sleeping and then compare the distribution of children among these categories after treatment, preferably given double blind and allocated at random. In about half of the trials, Chi-square (χ^2) tests were used by authors to compare the numbers of children in test and control groups and in most of these cases the conclusions drawn by the authors are, in statistical terms, safe. It is sometimes possible to re-analyse the data in the other studies but sometimes the original data are missing or inconsistent.

J.O. Morgan-Hughes, FFARCS, Consultant, Department of Anaesthetics, Norfolk and Norwich Hospital, St. Stephen's Road, Norwich NR1 3SR, J.A. Bangham, PhD, Lecturer, School of Biological Sciences, University of East Anglia, Norwich NR3 7TJ.

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Table 1. Placebo-controlled trials of sedative premedication in children.

Drug group	Drug	Reference
Phenothiazine	Trimeprazine	12,13,15,16,25,30,31
	Promethazine	10,11,24
	Trifluopromazine	11
	Pecazine	16
Benzodiazepines	Diazepam	17,19,20,24,25
	Flunitrazepam	21,22
	Lorazepam	25,33
	Midazolam	29,32,34,35
	Temazepam	30
Barbiturates	Pentobarbitone	3,8,11,13,19,21,22
	Secobarbitone	14
	Quinalbarbitone	15
Opioid analgesics	Morphine	3,4,11,14,29
	Pethidine	3,14,17,20
	Pentazocine	20,23
	Nalbuphine	23
Other drugs	Chloral hydrate	10
	Methylpentynol	10,16
	Droperidol	17,18
	Hydroxyzine	24
	Nefopam	28
Mixtures	Opioid analgesic and hyoscine	4,9,12,13,18
	Opioid analgesic and barbiturate	26
	Opioid analgesic and benzodiazepine	27
	Others	4,8,9,12,13,15,18,32

The most common way for authors to make an unsound statistical analysis was to assign ordinal values (1, 2, ...) to categories (asleep, drowsy, ...), average the values and compare the averages using statistical methods such as *t*-tests and ANOVA *F* tests. These tests are powerful only if it is possible to assume that the values are distributed normally, but some of the data demonstrate clearly that arbitrary scores of this type are not.

It was sometimes difficult to check the statistics because the number in each category was converted to a percentage. In some cases, 'fractional' children, outside the likely rounding errors, e.g. 55% of 10 children, were included.[29] Furthermore it is sometimes not clear whether the transformation to percentages had been accounted for in the statistical test. The Chi-squared test is based on counts in different categories and so it is not necessary to convert to percentages, a transformation that can be misleading. For example, a Chi-squared test comparing two categories with a total of 10 children may reveal no significant difference, whereas the same test applied to percentages, which implies 100 children, may reveal an apparent difference.

Where possible, in the following summary, the statistic is given as, for example, $\chi^2 = 20$ together with the probability of the statistic arising by chance on the assumption that there is no difference between the categories (the null hypothesis). A significant difference is assumed to arise when the probability is less than 0.05 (5% level). Statistical tests other than those applied by the authors are indicated in the text.

Results

Phenothiazines

Trimeprazine. Trimeprazine has had considerable popularity among British anaesthetists since the description in 1959 of the pre-operative use of the drug by Cope and Glover.[36]

Gillet and Kell[12] compared trimeprazine to a placebo but the trial was not randomised or blind and there was no statistical analysis.

McCloy and Riddoch[13] compared the pre-induction behaviour of 238 children given atropine alone by intramuscular injection with that of children given a variety of sedative drugs including oral trimeprazine 4.4 mg/kg with intramuscular atropine. The observers were unaware of the premedication but the allocation of patients to treatment groups was not randomised. Unsedated children under 6 years of age were significantly less frequently calm than older children ($\chi^2 = 28.7$, $p \approx 0$, re-calculated). In the younger age group 12 out of 46 children given trimeprazine were judged to be calm compared to 23 out of 125 children given atropine alone. This difference is not statistically significant.

Binning *et al.*[15] compared the behaviour in the anaesthetic room of four groups of children aged 2 to 8 years. The children in one group were given oral atropine alone and those in one of the sedated groups were given oral trimeprazine 4 mg/kg with atropine 1.5 hours before inhalational induction of anaesthesia. Children who were amenable and cooperative, whether they were awake or drowsy, were classified as 'good'. Ninety-six of 135 children in the trimeprazine group and 41 of 81 children in the atropine group were 'good'. No mention is made of the statistical test used, but if the Chi-squared test is applied to their data then this result is significant ($\chi^2 = 9.7$, $p \approx 0$, re-calculated). Unfortunately the four preparations were labelled A,B,C,D throughout the trial. The authors comment on the danger that the observers may in time know the contents of the preparations so that the trial was not strictly blind. Furthermore the method of allocation of the children to the

treatment groups is not mentioned and the preponderance of patients in the preferred trimeprazine group suggests that it was not random.

Doughty[16] reported a substantial blind, randomised comparison of oral trimeprazine 4.4 mg/kg and hyoscine 0.03 mg/kg with hyoscine alone. A child's behaviour in the anaesthetic room was deemed satisfactory if the child did not appear apprehensive, noisy or tearful, did not respond to intravenous induction by crying or being uncooperative and did not reflexly withdraw the hand. Only 66 of 120 children given trimeprazine were satisfactory compared to 84 of 120 in the unsedated group. This difference is significant ($\chi^2 = 5.76$, $p < 0.02$). More children in the trimeprazine group were sleepy but more were noisy. The difference is even more marked when children under the age of 7 years are considered separately. Doughty showed that trimeprazine conferred some amnesia for the events in the anaesthetic room, delayed recovery from anaesthesia and reduced the incidence of postoperative vomiting.

Burtles and Astley[25] studied four groups of 25 children in a blind randomised trial of oral trimeprazine, two benzodiazepines and a placebo. Nineteen children in the trimeprazine group and 13 children in the placebo group were calm at induction of anaesthesia. This difference is not statistically significant at the 5% level.

Padfield *et al.*[30] compared 28 children given oral trimeprazine 4 mg/kg with 27 given a placebo in a randomised double-blind trial which also included a group given temazepam. The approach to the assessment of the children's behaviour differs from earlier studies of trimeprazine in that they employed a scoring system (Table 2). The attraction of scoring systems is that they allow the use of more powerful statistical tests with which significant differences may be demonstrated with smaller numbers of patients. Padfield *et al.* used the Mann–Witney *U* test and found a highly significant difference between the scores of the trimeprazine group and the placebo group. However, the level of measurement must be at least ordinal for the application of the Mann–Whitney *U* test to be legitimate. It could be argued that the difference between 'sleeping' and 'awake' is a measure of hypnosis whereas the difference between 'awake' and 'crying' is a measure of anxiety. If this argument is accepted then there is no ordinal relationship between the three terms, and statistics alone are not enough to redeem the situation. In this study more children were asleep after trimeprazine but the frequency of crying and struggling was greater in the trimeprazine group than in the placebo group. These results are compatible with those of Doughty[16] and the different conclusion arises from the way in which the results have been considered.

Johnson and Young[31] reported, in a letter, a double-blind placebo-controlled trial of very low doses of oral trimeprazine for day-case surgery in two groups of 50 children. More children cried in the trimeprazine group than in the placebo group. The difference is significant ($\chi^2 = 4.51$, $p < 0.05$).

Table 2. Attitude on arrival in the anaesthetic room.

3 = Sleeping but rousable
2 = Sedated
1 = Awake
0 = Crying and struggling

In summary, trimeprazine in sufficient dose increases the proportion of children who are asleep or drowsy in the anaesthetic room but there is evidence that the frequency of crying and struggling at induction is increased by the use of this drug.

Promethazine. Freeman and Bachman[11] compared the behaviour of 23 children given atropine and promethazine 1.1 mg/kg by intramuscular injection with that of 27 children given atropine alone in a randomised blind trial. They made the comparison using a multiple comparison of means that is inappropriate to nonparametric data. They did not publish data which allowed the application of more appropriate tests, and no conclusions can be drawn.

Rollason[10] found no significant pre-operative differences between 101 children given promethazine 0.8 mg/kg orally and a control group given no premedication.

Desjardins *et al.*[24] compared oral promethazine 0.5 mg/kg with a placebo in a blind randomised trial. They showed no statistically significant differences for any of the factors examined between 40 children given promethazine and 36 given the placebo.

Other phenothiazines. Triflupromazine[11] and pecazine[16] have been included in placebo-controlled trials of premedication for children but these drugs are no longer available in the United Kingdom.

Benzodiazepines

Diazepam. McGarry[17] compared the level of consciousness and acceptance of the mask during inhalational induction of children premedicated with diazepam 0.4 mg/kg or a placebo. The route and timing of administration were not recorded. Analysis of variance (*F* test) was used to test the significance of differences between level of consciousness scores, but this is inappropriate unless it can be shown that the scores are normally distributed in each group. When Chi-squared tests are applied to the number of patients in each group there are no significant differences between diazepam and placebo ($\chi^2 \approx 1$, $p \approx 1$, recalculated: strictly there are too few patients but the conclusion is the same with the Fisher exact test).

Barker and Nisbet[19] compared several drugs including oral diazepam 0.2 mg/kg with placebo in children aged 2 to 17 years. They used a scoring system which graded the child's demeanour, response to intravenous induction and changes in heart rate and blood pressure. However, their histogram (Fig. 1) shows that the scores are not normally distributed about a mean and should not be compared

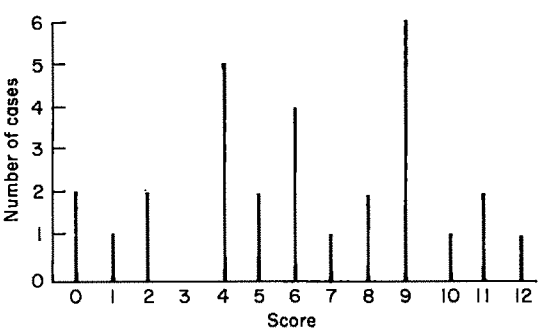

Fig. 1. Distribution of scores in children given a placebo, from Barker and Nisbet.[19]

using *t*-tests. Re-analysis of the data yielded no difference between test and control ($\chi^2 = 3.33$, $p = 0.7$).

Desjardins *et al.*[24] assessed the emotional state on arrival in the operating room of children aged 1 to 12 years. Twenty-one of 36 children given a placebo were serene, compared with 28 of 37 children given 0.1 mg/kg diazepam orally 1 hour earlier. This difference is not statistically significant. This result is consistent with the view that diazepam conferred no benefit. However, the number of patients was small.

The problem of small trials is also evident in the study of Burtles and Astley[25] who studied groups of 25 children aged 5–13 years. Twenty-two children were calm before induction in the group given oral diazepam 2.5 mg/kg compared to 13 in the placebo group. The children were also assessed before administration of the premedication. Random allocation of the children to the treatments failed to produce comparable groups since 86% of the 25 children (21.5 children!) who were later given diazepam were calm, compared to 15 children who were given placebo. It is not possible, therefore, to draw any conclusion about the calming effect of diazepam.

Iisalo and Iisalo[20] compared the pre-induction status of groups of 48 children aged 7 months to 12 years. Thirty children were calm and 18 were excited in the control group, who were given intramuscular saline; in the group given diazepam 0.2 mg/kg by intramuscular injection 39 children were calm and nine were excited. This difference is statistically significant ($\chi^2 = 4.1$, $p < 0.05$, recalculated). The number of children who were excited at induction was significantly lower in the diazepam group.

There is therefore evidence that intramuscular diazepam is preferable to intramuscular saline and that, by collecting the evidence from the small trials of oral diazepam, one can see a possibility that it too has a small effect.

Lorazepam. Burtles and Astley[25] and Van De Velde *et al.*[33] compared the pre-induction emotional status of children given oral lorazepam with that of children given a placebo and neither claimed significant differences.

Flunitrazepam. A study by Govaerts[21,22] in which rectal flunitrazepam is compared to a placebo as premedication for children is reported without data.

Midazolam. Rita *et al.*[29] studied 30 children in each of the age groups 1–5 years, 6–10 years and 11–15 years. Each child was allocated randomly to receive intramuscularly either midazolam 0.08 mg/kg, morphine 0.15 mg/kg or midazolam vehicle. There were, therefore, approximately 10 children in each study group. The degree of sedation was scored on a six-point scale and the quality of inhalational induction was scored on a four-point scale. Analysis of variance (ANOVA) was used as a test of the significance of differences in the scores between the treatment groups and the authors concluded that midazolam had significant advantages in the 1–5 year age group. However, analysis of variance cannot be applied legitimately when the level of measurement is, at best, ordinal. Comparison of the groups with a χ^2 or with a Fisher exact test reveals no difference at the 5% level, although it is difficult to conduct re-evaluation of this study as the proportion of patients in each behaviour category are shown as a percentage of the number in each treatment group and calculation of the actual number in each category reveals fractional people.

Payne *et al.*[32] reported a placebo-controlled study of midazolam 0.1 mg/kg by intramuscular injection in children aged 6 months to 5 years. Three of 50 children were crying in the holding area compared to nine in the placebo group. This difference is not significant at the 5% level ($\chi^2 = 3.4$, re-calculated). There were no differences between the groups at induction.

Feld *et al.*[34] report a study in which two dosage levels of oral and intramuscular midazolam were compared with midazolam vehicle. There were six study groups, each of 14 children aged 1 to 10 years. Oral midazolam had no significant effect. Two of 14 children in the intramuscular unsedated control group were calm or sleepy on arrival in the operating room compared to 12 of 14 who had received intramuscular midazolam 0.2 mg/kg. This difference is statistically significant ($\chi^2 = 14.4$, $p < 0.01$, recalculated). However, the control group showed an abnormally high level of unsatisfactory behaviour compared with controls in other studies (Tables 3a and b).

Wilton *et al.*[35] compared the sedative effect of intranasal midazolam 0.2 mg/kg or 0.3 mg/kg with that of isotonic saline administered to children aged 18 months to 5 years. The intranasal route was chosen to avoid first-pass metabolism by the portal circulation because midazolam has a high hepatic clearance. The 15 children in each group were assessed at 2.5-minute intervals up to 10 minutes, when they were separated from their parents, and then re-assessed in the operating room at 15 minutes during inhalational induction of anaesthesia. Behaviour was scored on a five-point scale. However, the terms agitated, alert, calm, drowsy and asleep do not constitute an ordinal scale, a problem that is not solved entirely by using the Kruskal–Wallis analysis of variance, even though this test does not depend on assumptions about the distribution of the data. The children given midazolam were more sedated after separation from their parents and at induction of anaesthesia than children given saline and these differences were statistically significant ($p < 0.05$).

Temazepam. Padfield *et al.*[30] showed no significant differences between the pre-operative behaviour of 29 children given oral temazepam 1 mg/kg and that of 27 children given a placebo.

Placebo-controlled studies of benzodiazepines for pre-operative medication of children are sufficiently encouraging to warrant further investigation, but the evidence of benefit is not strong enough to justify studies without placebo control. Either the effect is weak, or only a proportion of children are susceptible; in either case, careful controls and larger numbers of children will be required to allow the modest effect to be discriminated.

Barbiturates

Eckenhoff[8] reported a placebo-controlled trial of barbiturates for premedication of children in 1953, but the first blind randomised placebo-controlled trial was that of Freeman and Bachman[11] in 1959. However, these authors applied inappropriate statistical tests and no data can be extracted to allow statistical re-examination.

McCloy and Riddoch[13] conducted a blind but not randomised trial and reported a frequency of calm behaviour of 21 out of 49 children aged 5 years and under, who were premedicated with atropine and pentobarbitone 5 mg/kg by injection, compared to 23 out of 125 children in the same age group given atropine alone. This difference is statistically significant at all levels. They found, however,

Table 3a. The frequency of satisfactory behaviour in blind randomised trials of unsedated children after oral premedication.

Reference	Definition of satisfactory	Premedication	Age (years)	Size of group	Percentage satisfactory
Desjardins *et al.*[24]	Serene, adequately smooth induction	Placebo	1–12	36	58
				36	58
Burtles and Astley[25]	Calm	Placebo	5–13	25	52
Wilkinson[28]	As Doughty[9]	Placebo	4–13	23	83
Brzustowicz *et al.*[27]	Not crying	Placebo	5.4* (4.5)	77	66
Padfield *et al.*[30]	Not crying, well behaved at induction	Placebo	4–9	27	93
				27	70
Johnson and Young[31]	As Doughty[9]	Placebo	1–12	51	84
Payne *et al.*[32]	Not crying	Atropine	<5	50	72
Van de Velde *et al.*[33]	Not crying	Placebo	1–12	10	80

*mean (SD).

Table 3b. The frequency of satisfactory behaviour in blind randomised trials of unsedated children after intramuscular or subcutaneous premedication.

Reference	Definition of satisfactory	Premedication	Age (years)	Size of group	Percentage satisfactory
Doughty[9]	See text	Atropine	2–6	62	50
			7–12	44	68
Buckman[4]	Quiet or sleepy	Atropine	1–14	164	68
Davies and Doughty[18]	As Doughty[9]	Saline	2–6	87	61
			7–12	33	64
Iisalo and Iisalo[20]	Alert or drowsy	Saline	<12	48	62
Rita *et al.*[23]	Calm	Saline	<4	76	47
			5–9	146	57
	Smooth induction		<4	76	34
			5–9	146	61
Walters *et al.*[28]	Not excited	Atropine and oral placebo	>1	19	95
Feld *et al.*[34]	Sleepy or calm	Atropine and oral placebo	5.0 * (2.3)	14	15
		Placebo and oral atropine	3.6 (2.0)	14	29

*mean (SD).

that the percentage of children who showed disturbed or turbulent behaviour in the postoperative period in the pentobarbitone group was double that in the control group.

Eger *et al.*[3] studied the degree of fretfulness and irritability both before and after premedication, and the response to inhalational induction, in children given either pentobarbitone 2.2 mg/kg with an anticholinergic drug or the same anticholinergic drug alone. The route of administration of the drugs is not recorded. The proportion of children who showed a decrease in fretfulness and irritability after pentobarbitone was not significant. They confirmed the observation by McCloy and Riddoch[13] that there is a significant difference in the behaviour of children aged 5 years and younger compared to that of older children; the latter are more commonly calm.

Rackow and Salanitre[14] reported a comparison of intramuscular hyoscine and secobarbitone at three dosage levels with hyoscine alone. Each treatment group contained about 100 patients. The behaviour of the children before induction of anaesthesia was divided into three categories: A, crying or apprehensive; B, awake and calm; C, asleep. They demonstrated a statistically significant dose-effect relationship; the proportion of children who were crying or apprehensive diminished, and the proportion who were asleep increased, with increasing dosage of secobarbitone. However the highest percentage of children who were calm and awake was in the group which received hyoscine alone.

Binning and Watson[15] included oral quinalbarbitone 6 mg/kg among the drugs studied in a trial to which reference has already been made. Two-thirds of the children were asleep before induction of anaesthesia but those who were awake were 'difficult and intractable'.

It is reasonable to conclude that barbiturates reduce the frequency with which children cry in the anaesthetic room by increasing the proportion of children who are asleep. They do not increase the frequency of calm behaviour in those who are awake.

Opioid analgesics

Morphine. Eger *et al.*[3] recorded a decrease in the irritability and fretfulness of 20 of 33 children aged 5 years or less given morphine 0.175 mg/kg and an anticholinergic

compared to eight of 31 children given the anticholinergic drug alone. This difference is statistically significant ($\chi^2 = 6.0$, $p < 0.05$, recalculated). The route of administration is not recorded. The children in the morphine group vomited significantly more frequently in the recovery ward.

Rackow and Salanitre[14] compared children given morphine (at one of three doses by intramuscular injection with hyoscine) with children given hyoscine alone. The proportion of children who were awake and calm and the proportion who were asleep increased with increasing dose of morphine. The differences between the groups given morphine 0.11 mg/kg or 0.22 mg/kg and the control group were not significant. However, 13 of 89 children given morphine 0.33 mg/kg were apprehensive, 67 were calm and 10 were asleep while in the control group 34 of 102 children were apprehensive ($p < 0.001$). The authors found that the highest dosage level was associated with prolonged inhalational induction and slow recovery from anaesthesia.

Buchmann[4] compared 174 children aged 1–14 years given morphine 0.15 mg/kg by intramuscular injection, with atropine, to 164 children given atropine alone. Behaviour before induction of anaesthesia was categorised as apprehensive, quiet or sleepy. The largest difference between the treatments was in the quiet category, which included 80 children who had received morphine and 64 who had not. This difference is not statistically significant. There were no significant differences between groups in the frequencies of postoperative vomiting or recovery times.

Rita *et al.*[29] found no significant difference between the pre-operative behaviour of 11 children given intramuscular morphine 0.15 mg/kg and those given midazolam vehicle.

There is evidence that morphine in sufficient dose reduces the frequency with which children show signs of apprehension before induction of anaesthesia and that this is achieved partly by increasing the proportion who are asleep and partly by increasing the proportion who are awake but calm. However, inhalational induction may be prolonged and recovery delayed, and postoperative vomiting is more frequent.

Pethidine. Eger *et al.*[3] noted a reduction in pre-operative 'fretfulness and irritability' in 16 of 33 children aged less than 6 years who were given pethidine 1.7 mg/kg and an anticholinergic compared to eight of 31 children given the anticholinergic drug alone. This difference is not statistically significant at the 5% level ($\chi^2 = 3.50$, recalculated).

Rackow and Salanitre[14] examined the pre-operative behaviour of children who were given either hyoscine alone, or one of three doses of pethidine with hyoscine, by intramuscular injection. Each treatment group contained about 100 patients. There was little difference between the behaviour of 104 children given pethidine 2.2 mg/kg and that of 92 given 3.3 mg/kg. In each of these groups more than 80% of the children were either calm or asleep, significantly more than the 66% in the control group. Seventy-six percent of children in the group given 1.1 mg/kg were calm or asleep.

McGarry[17] compared level of consciousness and acceptance of the mask between two groups of children who received pethidine 1.1 mg/kg with atropine or atropine alone. The use of χ^2 tests on the data show that there were no significant differences between groups.

Iisalo and Iisalo[20] found 38 of 48 children given pethidine 1.0 mg/kg by intramuscular injection to be calm or asleep before induction compared to 30 of 48 given a placebo. These frequencies are similar to those reported by Rackow and Salanitre.[14]

Pentazocine. The proportion of children reported by Iisalo and Iisalo[20] to be calm or asleep after intramuscular pentazocine 0.9 mg/kg was the same as that after pethidine 1.0 mg/kg but more children were asleep or drowsy in the pentazocine group. The difference in the number of drowsy or asleep children in the pentazocine group was significantly greater than in a placebo group ($p < 0.01$). The time to awakening after operation was less in children given pentazocine than after placebo and there was no difference in the number of children who vomited in the recovery ward. The mean respiratory rate in the recovery ward was significantly less after pentazocine than after pethidine ($p < 0.05$) or placebo ($p < 0.001$).

Rita *et al.*[23] compared the pre-operative behaviour of 122 children aged less than 9 years who were given pentazocine 0.8 mg/kg with that of the same number given a placebo. Ninety-four children in the pentazocine group were calm compared to 62 in the placebo group, a highly significant difference ($p < 0.001$). In this paper 'calm' is defined as 'quiet, sedated or sleepy'.

Nalbuphine. Rita *et al.*[23] found a statistically significant difference between the number who were calm in a group of 125 children age 10 months to 14 years given nalbuphine and the number who were calm in a placebo group. However, 61% of those given nalbuphine were calm in the under-5 age group compared to 72% aged 5 to 9 years and 81% over 9 years. A significantly higher proportion of older children were given nalbuphine than placebo ($\chi^2 = 11.38$, $p < 0.005$, recalculated). The difference between the treated group and the placebo group may be accounted for by the different age distribution.

There is good evidence that morphine, pethidine and the partial agonist pentazocine administered by intramuscular injection are associated with a higher incidence of calm or sleepy children than occurs in children given a placebo by intramuscular injection. However, this does not answer the question 'Are intramuscular opioids better than nothing at all?' since children in the placebo groups were subjected to an intramuscular injection.

The definition of satisfactory behaviour varies among studies, but, when the results from unsedated control groups are pooled the frequency of satisfactory behaviour of those given premedication by injection (Table 3b) is significantly lower than those given oral premedication (Table 3a; $\chi^2 = 18.7$, $p \approx 0$).

Other drugs

Droperidol. The application of χ^2 to McGarry's data[17] demonstrates that the pre-operative effects of droperidol 0.05 mg/kg were not significantly different from those of a placebo. The route of administration was not recorded.

Davies and Doughty[18] compared intramuscular droperidol 0.22 mg/kg with intramuscular saline 0.9% given to groups of 120 children. There were no significant differences in pre-operative demeanour or response to intravenous induction.

Hydroxyzine. Desjardins *et al.*[24] compared the emotional state on arrival in the anaesthetic room, and the response to induction, of 43 children given oral hydroxyzine 0.5 mg/kg with that of 36 patients given a placebo. Thirty-seven children were serene on arrival in the hydroyzine group

compared to 21 in the placebo group. This difference is significant ($\chi^2 = 8.0$, $p < 0.005$). However, there was no significant difference in the response to induction between the two groups and the authors concluded that hydroxyzine conferred no benefit.

Nefopam. Wilkinson[28] reported a placebo-controlled trial of nefopam which was abandoned because of the incidence and severity of postoperative vomiting.

Chloral hydrate. Rollason[10] presented data from a placebo-controlled trial of chloral hydrate in the discussion which followed a paper by Doughty at the Royal Society of Medicine in 1959. He reported no significant differences between chloral hydrate and placebo. Triclofos and other more palatable formulations of chloral hydrate have been compared favourably to diazepam[37,38] flunitrazepam[38] and midazolam.[39]

Mixtures

Opioids with hyoscine. A mixture of papaveretum 0.5 mg/kg and hyoscine 0.01 mg/kg administered by subcutaneous injection 90 minutes before operation was compared to atropine alone by Doughty.[9] The behaviour was defined as satisfactory if the child was not tearful or noisy on arrival in the anaesthetic room and did not withdraw the hand, cry or respond violently to venepuncture. The behaviour was satisfactory in 70 of 106 children in the atropine group and 91 of 106 in the papaveretum and hyoscine group. This difference is highly significant ($p < 0.001$). However, a change in the definition to include apprehensive appearance as unsatisfactory behaviour results in no significant difference between the two groups.

A similar result was obtained when Davies and Doughty[18] compared a smaller dose of papaveretum and hyoscine with saline 0.9% by intramuscular injection. They noted excessive salivary suppression and a tendency to repeated and persistent postoperative vomiting after papaveretum and hyoscine. The behaviour of 74 of 120 children given intramuscular saline was satisfactory and the authors expressed the view that there should be little ethical objection to using normal saline as a control.

Buchmann[4] compared the pre-operative appearance and response to induction of 163 children aged 1 to 14 years given intramuscular morphine 0.15 mg/kg and hyoscine 0.01 mg/kg with that of 174 children given atropine alone. Thirty-eight of the children who received papaveretum and hyoscine were apprehensive compared to 50 in the atropine group. This difference is not significant.

McCloy and Riddoch[13] showed no significant pre-operative differences between children given pethidine and hyoscine and those given atropine alone.

Opioid and barbiturate. Eckenhoff[8] described the use of a mixture of pentobarbitone, morphine and hyoscine in a placebo-controlled trial which was not blind or randomised.

Walters *et al.*[26] report a study designed primarily to compare intramuscular with oral premedication. The control group received two injections of atropine and an oral placebo. The intramuscular group received morphine 0.1 mg/kg and pentobarbitone 4.0 mg/kg by two intramuscular injections, and the oral placebo. The oral group received atropine by two intramuscular injections and pentobarbitone 4.0 mg/kg and pethidine 3.0 mg/kg orally. The authors assert that there was no statistical difference between the control group and another control group used in another, earlier, study and so combined them. The statistical evidence was not reported. However, they showed that both premedicated groups were more drowsy than the unpremedicated groups. There was no difference between the intramuscular and oral groups ($p = 0.15$).

Opioid and phenothiazine. McCloy and Riddoch[13] reported a negative trial of pethidine and promethazine versus a placebo.

Buchmann[4] compared 176 children given pethidine 1.4 mg/kg and promethazine 0.35 mg/kg by intramuscular injection with 174 children given atropine by the same route. Thirty-four of the children given the mixture were apprehensive compared to 50 in the control group. This difference is significant at the 5% level ($\chi^2 = 4.1$).

Opioid and benzodiazepine. Brzustowicz *et al.*[27] studied 81 children given pethidine 1.5 mg/kg, diazepam 0.2 mg/kg and atropine 0.02 mg/kg orally, and 77 children given a placebo. Twenty-six (34%) of the children in the placebo group and 15 (19%) of the test group were crying on arrival in the operating room. This difference is statistically significant ($\chi^2 = 4.73$, $p < 0.05$, recalculated). The attitude to inhalational induction was also compared, but the sedative mixture appeared to confer no benefit.

Opioid and droperidol. Davies and Doughty[18] found no advantage when a mixture of droperidol and phenoperidine was compared to intramuscular saline.

Opioid, phenothiazine and droperidol. Payne *et al.*[32] compared the pre-operative behaviour of children given a mixture of methadone, trimeprazine, droperidol and atropine with that of a similar group who were given atropine alone and found no significant difference.

Discussion

Oral administration

Oral trimeprazine in sufficient dose increases the proportion of children asleep before induction of anaesthesia but those who are awake are more likely to be noisy or crying.[16,31]

In most trials of oral benzodiazepines the frequency of calm behaviour is higher than in the unsedated control groups, but none show statistically significant benefit. These drugs may be of value but the effect at the doses that have been used is too small to be demonstrated by the small trials which have been published.

Studies which compare triclofos with oral benzodiazepines show triclofos to be significantly more effective[37-39] but a placebo-controlled trial of triclofos does not appear to have been published.

Oral barbiturates increase the proportion of children who are asleep before induction of anaesthesia but those who are awake are more likely to behave unsatisfactorily.[15]

A mixture of oral pethidine and diazepam reduces the frequency of crying on arrival in the anaesthetic room but confers no benefit at inhalational induction.[27]

Intramuscular administration

Diazepam 0.2 mg/kg by intramuscular injection increases the frequency of calm behaviour both before and at induction when compared to intramuscular saline.[20] There is

some evidence that intramuscular midazolam 0.2 mg/kg may also be effective.[34]

Intramuscular barbiturates reduce the number of children who cry or are apprehensive before induction of anaesthesia by increasing the proportion who are asleep but may reduce the number who are calm among those who are awake.[14]

Intramuscular opioid analgesics either alone or in combination with other sedative drugs, have repeatedly been shown to reduce the number of children who cry at induction of anaesthesia when compared to intramuscular placebos. This effect is the result of an increase in the number of children who are asleep and the number who are awake but calm.

Administration by other routes

The search revealed no placebo-controlled trials of rectal administration of sedative premedication in children from which any conclusion could be drawn.

Intranasal midazolam 0.3 mg/kg increases the proportion of children who are calm or asleep at induction 15 minutes after administration.[35]

Design of trials

A formula for estimating the number of children that should be included in a trial is given in the appendix.

The incidence of calm behaviour at induction of anaesthesia of unsedated younger children is lower than that in children aged 6 years. Thus, the benefit of premedication is more likely to be revealed by study of younger children. Placebo controls in studies of the effects of premedication on the behaviour of children are necessary.

Appendix

Statistical method for determining trial size for a qualitative outcome.[40] The required number of patients on each treatment, n, is given by the following formula:

$$n = \frac{\{Pc\,(100-Pc)+Pt\,(100-Pt)\}}{(Pt-Pc)(Pt-Pc)}.f\,(\alpha,\,\beta)$$

where Pc = percentage of successes expected in the control group

Pt = percentage of successes in the treatment group.

α (type 1 error) is the probability of detecting a significant difference using the χ^2-test when the treatments are really equally effective. Often set at 0.05, it represents the risk of a false positive result.

β (type 2 error) is the probability of not detecting a significant difference when there really is a difference of the magnitude (Pt-Pc). Often set at 0.1, it represents the risk of a false negative result.

The values of $f(\alpha,\beta)$ are shown in Table 4.

Table 4. Values of $f(\alpha,\beta)$ to be used in formula for required number of patients.[40]

		β (type 2 error)			
		0.05	0.1	0.2	0.5
α (type 1 error)	0.1	10.8	8.6	6.2	2.7
	0.5	13.0	10.5	7.9	3.8
	0.02	15.8	13.0	10.0	5.4
	0.01	17.8	14.9	11.7	6.6

Acknowledgment

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Omeprazole for prophylaxis of acid aspiration in elective surgery

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Summary

The aim of the study was to determine whether a single oral dose of omeprazole 40 mg is effective in increasing the pH of gastric residue above 2.5 at the time of anaesthetic induction in adult patients scheduled for elective gynaecological surgery. The patients were allocated to receive either chlorazepate dipotassium 25 mg alone or omeprazole 40 mg and chlorazepate dipotassium 25 mg on the night before surgery. Gastric volume and pH were measured after induction of anaesthesia. Patients who received omeprazole had a higher mean pH than control patients ($p < 0.001$). The pH was less than 3.5 in 50% of patients in the control group, but in only 4.5% of those who received omeprazole ($p < 0.01$). Mean (SEM) volume of gastric fluid was 15.2 (2.7) ml in the control group and 9.2 (1.8) ml in the omeprazole group, but the results were not statistically significant. A single dose of 40 mg omeprazole significantly decreased the number of patients at risk of aspiration pneumonitis.

Key words

Gastrointestinal tract; gastric pH, gastric volume.
Pharmacology; omeprazole.

The danger of pulmonary aspiration is always of concern to anaesthetists. Between 30 and 50% of patients scheduled for elective surgery after a fasting period of more than 8 hours have a gastric volume greater than 25 ml[1–3] and an even greater percentage (64–82%) have a gastric pH less than 2.5.[2–3] Several attempts have been made to eliminate the risk of pulmonary aspiration by altering the pH of gastric contents towards neutral. Antacids and H_2-receptor antagonists are employed with variable success. Cimetidine was investigated widely as a premedicant to increase the pH and decrease the volume of gastric contents.[3–5] However, some patients have a gastric pH of 2.5 or less after cimetidine and are potentially at risk of gastric aspiration.[2–4,5] Ranitidine, a more potent H_2-receptor antagonist, seems to be more effective than cimetidine in increasing gastric pH[6–8] but 8% of patients still have a pH less than 2.5 and 17% less than 3.5.[9] Omeprazole, a substituted benzimidazole, decreases gastric secretion by inhibiting the action of the proton pump H^+-K^+ ATP-ase, which exchanges luminal potassium for cellular hydrogen ions.[10] Omeprazole is more potent than H_2-receptor antagonists because it acts on the final step in the stimulatory process for acid secretion.[11] Numerous studies have shown almost total inhibition of gastric secretion and acidity with no detectable side effects in normal individuals and patients with duodenal ulcers after treatment with omeprazole.[12,13]

The aim of the study was to determine whether a single oral dose of omeprazole 40 mg is effective in increasing the pH of gastric residue above 2.5 at the time of induction of anaesthesia.

Methods

Forty-four adult patients (ASA 1 or 2) scheduled for elective gynaecological surgery were studied. Informed verbal consent was obtained from each patient, and the study was approved by the hospital's ethics committee. No patient had gastrointestinal disease or was taking drugs known to influence gastric acidity or volume. Obese patients were not included in the study (body weight 20% above the ideal weight was defined as obesity). Age, weight and fasting interval were recorded. All the patients had fasted for a minimum of 8 hours before induction of anaesthesia. Patients were allocated randomly to one of

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Table 1. Patients' characteristics. Data are presented as mean (SEM).

	Number of patients	Age (years)	Weight (kg)	Fasting interval (hours)
Group 1 (control)	22	36.8 (2.4)	60.3 (1.4)	10.7 (0.2)
Group 2 (omeprazole)	22	36.4 (2.7)	60.9 (1.8)	10.5 (0.5)

Table 2. Gastric pH and volume.

	pH mean (SEM) and range	% patients with gastric pH <3.5	Volume (ml) mean (SEM) and range	% patients with gastric volume >25 ml
Group 1 (control)	3.1 (0.5) 1.1–7.5	50	15.2 (2.7) 0–50	23
Group 2 (omeprazole)	5.9 (0.4) 2.4–7.8	4.5	9.2 (1.8) 0–50	9
Significance	$p<0.001$	$p<0.01$	NS	NS

NS, not significant.

two groups. Patients in Group 1 ($n = 22$) served as controls and received clorazepate dipotassium 25 mg orally at 2200 hours on the night before surgery. Patients in Group 2 ($n = 22$) received clorazepate dipotassium 25 mg together with omeprazole 40 mg orally at 2200 hours.

Induction of anaesthesia was accomplished with intravenous thiopentone 4–6 mg/kg followed by a neuromuscular blocking agent and tracheal intubation. Nitrous oxide and fentanyl were used for maintenance. A 16-FG Salem gastric tube was inserted into the stomach after induction of anaesthesia and available gastric contents were evacuated by a 50-ml syringe, after positioning the patient in various postures. The investigator who took the sample was unaware of the group to which the patient had been assigned. The volume was recorded and the pH measured using a Corning Digital pH meter.

Data were analysed using one-way analysis of variance and Student's *t*-test. Chi-square analysis was used to compare the proportions of patients in the two groups with pH < 3.5 and volume > 25 ml. Results were considered statistically significant if the p value was less than 0.05.

Results

The two groups were comparable in respect of age, weight and fasting interval (Table 1). There were no differences between groups in the incidences of smoking, heartburn or dyspepsia. Gastric contents could not be obtained from three patients in group 1 and five patients in group 2. Consequently, the pH data are not available for these eight patients.

The volume and pH of gastric fluid are shown in Table 2. Mean pH was higher in patients treated with omeprazole than in the control group ($p < 0.001$). Fifty percent of patients in the control group had a pH of less than 3.5 compared with 4.5% in the omeprazole group ($p < 0.01$). Mean (SEM) gastric volume was 15.2 (2.7) ml in the control group and 9.2 (1.8) ml in the omeprazole group but the difference was not statistically significant. Twenty-three percent of patients in the control group had a gastric volume in excess of 25 ml compared with 9% in the treated group. Figure 1 is a scattergram of volume and pH values in the two groups. Most of the values from the omeprazole

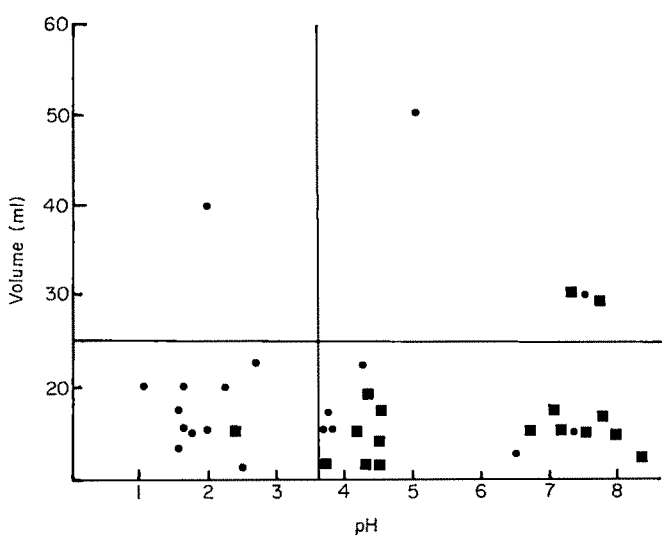

Fig. 1. Scattergram of volume versus pH in the control (●) and the omeprazole groups (■).

group fell in the safest area, i.e. low volume with high pH. Most of the values from the control group fell in the low pH area.

Discussion

Mendelson[14] and Teabeaut[15] have demonstrated the importance of pH in the aetiology of aspiration. A gastric pH below 2.5 and a volume of 25 ml or greater are considered critical factors for the development of pulmonary damage in adults.[16] According to this definition, 17 to 64% of elective adult patients who have been fasting are said to be at risk.[2-4] However, a higher percentage of patients coming for elective surgery are at risk if Crawford's suggestion of a limit of pH of 3.5 is accepted.[17] Omeprazole reduced significantly the number of patients at risk if aspiration should occur. Only one patient (4.5%) had a pH < 3.5 (pH = 2.4).

One possible explanation for the failure of omeprazole to increase the pH of the gastric contents to more than 3.5 in that patient is inadequate dosage. It is known that single oral administration of omeprazole 20–80 mg gives a dose-dependent inhibition of acid secretion of about 30 to 100% for 24–48 hours. A single dose of 40 mg reduces pentagastrin-stimulated acid output by 65%. The inhibition of gastric secretion is total (90%) with a single dose of 80 mg.[12-18]

Omeprazole did not reduce significantly the residual gastric volume. Sampling through a Salem sump tube may underestimate the total volume,[19] but there is a good correlation between volume aspirated and volume determined by indicator dilution.[20]

In conclusion, omeprazole was effective in reducing gastric acidity in adult patients scheduled for elective gynaecological surgery. A single oral dose of 40 mg decreased significantly the number of patients at risk of serious pulmonary damage. Further study of the effect on gastric pH and volume is indicated with a dose of 60 to 80 mg.

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Pain on injection of propofol

Methods of alleviation

R. A. JOHNSON, N. J. N. HARPER, S. CHADWICK AND A. VOHRA

Summary

A controlled randomised double-blind design was used to study the effect of lignocaine on the pain produced by intravenous injection of propofol. Patients received a 2-ml pretreatment solution with temporary venous occlusion, followed by an induction solution. One hundred and three patients were assigned to one of five groups: saline pretreatment, followed by induction with propofol plus saline 2 ml; lignocaine 20 mg pretreatment, followed by induction with propofol plus saline 2 ml; lignocaine 40 mg pretreatment, followed by induction with propofol plus saline 2 ml; saline pretreatment, followed by induction with propofol plus lignocaine 20 mg; or saline pretreatment, followed by induction with propofol plus lignocaine 40 mg. Pain was reduced significantly in all groups in which lignocaine was used and a dose of 40 mg was more effective than 20 mg. There were no significant differences in the incidence of pain among the groups which received lignocaine as pretreatment and the groups which received lignocaine mixed with propofol. Sixty-eight percent of patients who experienced pain or discomfort recalled it in the postoperative period.

Key words

Anaesthetics, intravenous; propofol.
Complications; pain, recall.

The use of the intravenous anaesthetic agent propofol has increased rapidly because of the high quality of anaesthesia and rapid recovery. A disadvantage of its use is the pain associated frequently with injection into small veins.[1–5] The pain is less after injection into a vein in the antecubital fossa,[1,4] but use of this site is associated with a risk of intra-arterial injection and is sometimes inconvenient.

Two possible approaches might reduce this discomfort: a local anaesthetic agent such as lignocaine may be mixed with propofol[1–3] or a local anaesthetic may be injected before propofol.[1,3,4] There is no previously published randomised double-blind comparison of these methods.

The aims of this study were to compare these techniques with injection of propofol alone, and to determine the most effective dose of lignocaine. In addition we investigated the postoperative recall of pain on injection.

Methods

The study design was approved by the hospital ethics committee. One hundred and three adult patients scheduled to undergo elective surgery were studied after they had given informed written consent. Patients of ASA groups 3–5 and those who suffered from cardiac conduction defects, epilepsy or took anti-arrhythmic drugs were excluded. A randomised controlled double-blind method of evaluation was used.

Patients were allocated randomly to one of five groups. Each patient received 2 ml of a pretreatment solution followed by an induction mixture (Table 1). All drug mixtures were prepared freshly by an anaesthetist but their contents were not known to the investigating anaesthetist.

All patients were premedicated with diazepam 10 mg one hour before operation. A 23-guage intravenous cannula (Y-can, Wallace) was inserted on the dorsum of the hand. No analgesic drug was given before induction. The patient was given 2 ml of the pretreatment solution over 5 seconds while the venous drainage was occluded manually at mid-forearm by an assistant.[6] The occlusion was released after 20 seconds and 4 ml of the induction solution was administered over 5 seconds. The patient was then asked 'is the injection comfortable?'. If any discomfort was indicated the patient was asked 'Is it unpleasant or painful?'. The degree and site of discomfort was noted.

Induction of anaesthesia was continued in all patients with propofol (total dose 1.5–3 mg/kg). Anaesthesia was maintained using an inhalational technique. Blood pressure and ECG were monitored during anaesthesia, and any

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Table 1. Patient groups: pretreatment and induction mixtures.

	Induction mixture		
Pretreatment (2 ml)	Propofol 200 mg plus saline 2 ml	Propofol 200 mg plus lignocaine 20 mg	Propofol 200 mg plus lignocaine 40 mg
Saline 0.9%	Group A	Group D	Group E
Lignocaine 1% (20 mg)	Group B		
Lignocaine 2% (40 mg)	Group C		

possible adverse effects of lignocaine were recorded. After recovery from anaesthesia the patients were asked if they had any recall of discomfort at induction.

The statistical significance of differences between groups was estimated by the Chi-square test or Fisher's exact test. Allowance was made for multiple comparisons. A p value of less than 0.05 was accepted as being significant.

Results

There were no differences among the groups with regard to age, weight or sex. We did not observe any adverse effects attributable to lignocaine during anaesthesia or any gross effects on the quality of recovery. The number of patients who experienced pain or discomfort in each group is shown in Table 2.

No lignocaine (group A)

More than half of the patients who received no lignocaine (59.1%) experienced pain and three patients (13.6%) experienced discomfort.

Lignocaine pretreatment (groups B and C)

Four patients (19%) in group B (lignocaine 20 mg) experienced pain and one patient (4.8%) experienced discomfort. These numbers were significantly lower than in group A, both with regard to pain ($p < 0.025$) and pain or discomfort ($p < 0.005$). Only one patient (5.3%) in group C (lignocaine 40 mg) experienced pain and no patient experienced discomfort. These incidences were also significantly lower than in group A ($p < 0.001$ for pain and $p < 0.0005$ for pain or discomfort). Groups B and C were not significantly different from each other.

Lignocaine mixed with propofol (groups D and E)

One patient (5.6%) in group D (lignocaine 20 mg) experienced pain and two patients (11.1%) experienced discomfort, significantly fewer than in group A both with regard to pain ($p < 0.005$) and pain or discomfort ($p < 0.0005$). No patient in group E (lignocaine 40 mg) experienced pain or discomfort. This was also significantly fewer than in group A ($p < 0.0005$ for pain and $p < 0.0005$ for pain or discomfort). Groups D and E were not significantly different from each other.

There was no difference in the incidence of pain or discomfort between groups B and D, who received lignocaine 20 mg by different methods. Similarly, there was no difference between groups C and E, who received lignocaine 40 mg by different methods.

The dose of lignocaine appeared to be more important than the method of administration. Significantly fewer patients in groups C and E (lignocaine 40 mg) experienced pain or discomfort (2.4%) than in groups B and D (20.5%; $p < 0.05$).

Figure 1 shows the incidence of recall amongst patients who experienced pain, irrespective of group, and Figure 2 shows the incidence of recall amongst patients who experienced discomfort, irrespective of group. Pain or discomfort was recalled by 14 (73.7%) of the 19 patients who experienced pain. Discomfort was recalled correctly by three (50%) of six patients. This difference suggests that the rate of accurate recall may be proportional to the intensity of the stimulus, although the difference is not statistically significant. No patient recalled a sensation worse than that experienced.

Discussion

Pain on injection of intravenous drugs is not considered usually as a serious complication of anaesthesia. However, it may be distressing to patients, and can reduce the acceptability of an otherwise useful agent. Administration of propofol into a small vein results in pain in the majority (59.1%) of patients, most of whom recall it (73.7%).

There have been previous studies of this problem and its management. A multicentre evaluation by Stark *et al.*[1] found that lignocaine 10 mg used either as a pretreatment or mixed with propofol reduced the incidence of pain from 28.5% to 8.8%, but they did not differentiate between the methods. Brooker *et al.*[2] found that pretreatment with

Table 2. The number of patients in each group who experienced an unpleasant sensation during injection of propofol.

Group	*n*	Pretreatment	Induction mixture	Discomfort	Pain
A	22	Saline	Saline plus propofol	3	13
B	21	Lignocaine 20 mg	Saline plus propofol	1	4
C	20	Lignocaine 40 mg	Saline plus propofol	0	1
D	18	Saline	Lignocaine 20 mg plus propofol	2	1
E	22	Saline	Lignocaine 40 mg plus propofol	0	0

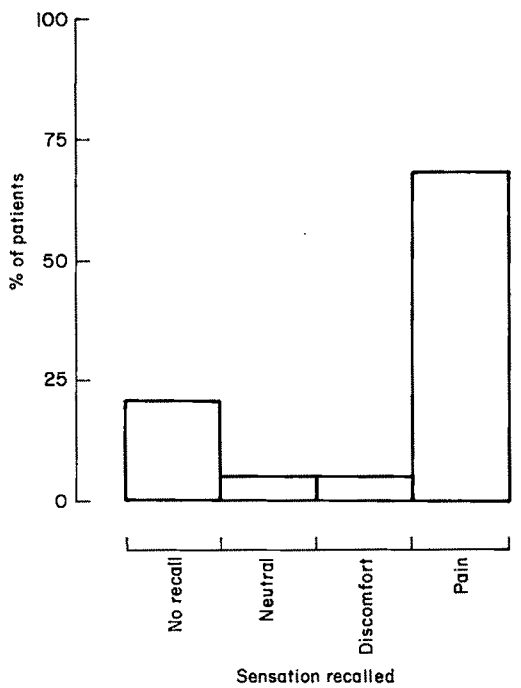

Fig. 1. Patients who experienced pain at induction: the percentage of patients who recalled nothing, a neutral sensation, discomfort or pain.

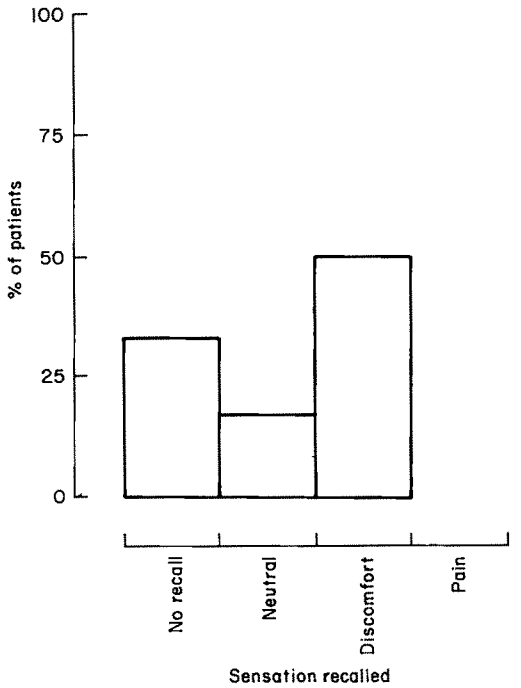

Fig. 2. Patients who experienced discomfort at induction: the percentage of patients who recalled nothing, a neutral sensation, discomfort or pain.

lignocaine 10 mg did not prevent pain, whereas lignocaine 7.5 mg in propofol 142.5 mg was effective. They confirmed this finding subsequently[7] and reported an incidence of pain of 3.7% in treated patients. However, some patients received premedication with papaveretum and all received alfentanil 250 μg before induction. The rate of injection of propofol was unusually slow, (approximately 1 ml per 10 seconds) and interpretation of their results is difficult. In contrast, McCulloch and Lees[4] found that the incidence of pain was reduced from 37.5% to 17.5% after pretreatment with lignocaine 10 mg, but this difference was not statistically significant.

Scott *et al.*[8], in a study of various techniques used to alleviate discomfort, found a reduction in the incidence of pain when propofol was mixed with lignocaine 10 mg. However, the number of patients studied was small. Helbo-Hansen *et al.*[9] used the same dose and technique, and found pain in 10 of 40 patients. Stokes *et al.*[10] used an alternative approach; they diluted propofol to 5 mg/ml with glucose 5%, but found moderate or severe pain in 12 of 50 patients. Studies in children have confirmed the reduction of pain by the addition of lignocaine 10 mg to propofol 200 mg, but the incidence of pain was still greater than that seen with thiopentone.[11–13]

Our investigation was designed to answer the following questions: is there a difference between pretreatment and mixing, and does the dose of lignocaine influence the incidence of pain or discomfort? We chose 40 mg as the maximum dose of lignocaine because it is less than half of the dose used to obtund the hypertensive response to intubation and is unlikely to be associated with adverse effects. The lower dose of 20 mg was selected because previous investigations suggested that 10 mg was unsatisfactory.

We confirmed that an unacceptably high incidence of pain or discomfort followed the injection of propofol alone. We strongly suggest the use of a technique which prevents this. Lignocaine 20 mg or 40 mg, given by either method, reduced discomfort in comparison with propofol alone. A dose of 40 mg was more effective than 20 mg, and we consider that this dose should be used.

The technique of administration did not influence the incidence of pain or discomfort. This choice must therefore depend on other factors. Pretreatment avoids the need to mix drugs, prevents pharmaceutical interactions and avoids dilution of the induction agent. Mixing has the advantage of reducing the dose of lignocaine administered if the induction dose of propofol is less than 200 mg, and is simpler in practice. The manufacturer's investigations suggest that propofol dissolved in lignocaine is stable if used immediately (ICI Pharmaceuticals, personal communication). Consequently, we believe that a mixture may be the method of choice.

The incidence of recall of pain or discomfort experienced during induction was high. This finding suggests that administration of propofol does not ensure amnesia of noxious events that occur during induction of anaesthesia.

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Pain on injection of propofol: the effect of injectate temperature

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Summary

A double-blind, randomised clinical study was undertaken to compare the effect of temperature on the incidence and severity of the pain experienced on injection of propofol. The number of patients who experienced pain and the severity of the pain were reduced significantly when propofol was administered at a temperature of 4°C. The efficacy of propofol as an induction agent appeared to remain unaltered.

Key words

Anaesthetics, intravenous; propofol.
Complications; pain.

It is well recognised that propofol may cause pain or discomfort on injection when administered intravenously, especially into a vein on the dorsum of the hand. Studies have shown that the incidence may be as high as 45%.[1] Premedication has little influence on the incidence of pain but may reduce its severity.[2] Other important factors are known to be the site and speed of injection[3–7] and the use of analgesics and local anaesthetics in combination with propofol.[7–9] This study was designed to assess whether the temperature of propofol affects the incidence or severity of pain on injection.

Patients and methods

The study was performed on 71 adult patients of ASA class 1 and weight 50–85 kg who presented for minor, elective surgery. Informed consent was obtained. All patients received lorazepam 0.5 mg/10 kg to a maximum of 4 mg, 90 minutes before surgery. A 22-gauge cannula was inserted into the largest apparent vein in the dorsum of the hand. The patients were then allocated randomly to one of two groups.

General anaesthesia was induced with intravenous propofol 2.5 mg/kg. Patients in group 1 received propofol that had been taken directly from the refrigerator (4–5°C). Those in group 2 received propofol maintained at room temperature (20–23°C). The speed of injection was controlled carefully. One quarter of the total calculated dose was given over the first 5 seconds; after this period, the injection was stopped for 5 seconds to allow assessment of discomfort by the method outlined below. An initial pain score was obtained. Induction was then continued and the second quarter of the total induction dose was administered over a further 5-second period. The patient was questioned again and a second pain score obtained. Finally, the remainder of the induction dose was administered.

The level of pain was assessed by a second, independent anaesthetist who was unaware of the group to which the patient had been allocated. The pain score was obtained by asking the patient a standard question about the comfort of the injection and the verbal response, together with behavioural signs such as facial grimacing, arm withdrawal or tears. A score of 0 to 3, which corresponded to no pain, mild, moderate and severe pain, respectively, was recorded (Table 1).

Results

The second pain score was higher in all cases and this score was used for later analysis. The results are shown in Table 2. The overall incidence of pain in group 2 was 46% compared with 23% in group 1 ($p < 0.05$). In addition, less patients in group 1 experienced severe pain (3% versus 21%; $p < 0.025$). Propofol induced anaesthesia successfully irrespective of temperature.

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Table 1. Assessment of pain.

Pain score	Degree of pain	Response
0	None	Negative response to questioning.
1	Mild	Pain reported in response to questioning only, without any behavioural signs.
2	Moderate	Pain reported in response to questioning and accompanied by a behavioural sign, or pain reported spontaneously without questioning.
3	Severe	Strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears.

Table 2. Pain assessments after administration of propofol at a temperature of 4–5°C (group 1) or at room temperature (group 2).

	0 No pain	1 Mild	2 Moderate	3 Severe
Group 1 $n = 34$	26	3	4	1
Group 2 $n = 37$	20	4	5	8

Significant difference between column 0 and columns 1+2+3 (overall incidence of pain) $p < 0.05$ (chi-squared test).

Discussion

The incidence of pain associated with injection of propofol at room temperature in this study was 46% which is similar to that in previous studies.[1] Our results indicate that propofol injected at a temperature of 4–5°C is associated with a reduced incidence of pain on injection.

Previous investigators have shown that the injection of propofol into a vein in the antecubital fossa is associated with a low incidence of pain.[3–7] However, this route is seldom used in clinical anaesthetic practice as the dorsum of the hand is more convenient and accessible during surgery. Brooker *et al.*[9] showed that freshly mixed propofol and 1% lignocaine reduced the incidence of pain on injection significantly. Other workers have shown that the addition of lignocaine may reduce the overall incidence of pain on injection into the dorsum of the hand to less than 9%.[7–8] These studies may not be directly comparable to ours because of the variations in premedication and the use of pre-induction opioids in some cases.

The datasheet supplied by ICI Pharmaceuticals recommends that propofol should be stored at room temperature; however, direct communication with the company has confirmed that propofol may be stored and administered at any temperature below 25°C provided that it is not frozen.

The exact mechanism for the production of pain with propofol injection remains to be elucidated. Some authors have implicated a kinin cascade,[7] which would result in a slight delay before pain is experienced. The second pain score in our study was always higher than the first if pain was experienced. The indirect biochemical cascade mechanism may be supported by our findings, in that biochemical reactions might be expected to occur less vigorously at lower temperatures, and may fail to reach pain threshold levels in some patients.

In conclusion, it appears that the use of propofol at 4–5°C may provide a simple and safe method of reducing the incidence of pain on injection without the addition of other pharmacological agents.

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Flumazenil in the outpatient

A study following midazolam as sedation for upper gastrointestinal endoscopy

P. J. D. ANDREWS, D. J. WRIGHT AND M. C. LAMONT

Summary

Fifty outpatients who underwent upper gastrointestinal endoscopy under midazolam sedation were allocated randomly into two equal groups of 25 in this double-blind study. After the endoscopy, and 30 minutes after administration of the sedative, patients in one group received flumazenil 0.5 mg; those in the other group received a similar volume of vehicle only. Assessments of memory function, psychomotor performance and coordination were carried out and these were repeated 3.5 hours later. Flumazenil produced a significant improvement ($p < 0.0001$) immediately but no difference could be detected between flumazenil and placebo at 3.5 hours. However, patients in the flumazenil group reported, by means of linear analogue scales, a subjective feeling of alertness at the time of discharge, which was greater than that reported by those in the placebo group ($p < 0.005$).

Key words

Gastrointestinal tract; endoscopy.
Pharmacology; midazolam, flumazenil.

Benzodiazepines are used commonly for intravenous sedation for outpatient diagnostic investigations. Midazolam produces excellent amnesia, anxiolysis and, if titrated carefully, minimal cardiorespiratory depression.[1] It also has the most suitable pharmacokinetic profile of the benzodiazepines for use in the outpatient.[2] The central effects of intravenous sedation with midazolam usually last longer than is necessary for the clinical investigation and thus recovery facilities and close nursing care may be required until the patient is fit to leave hospital. Flumazenil, an imidazobenzodiazepine, is an antagonist of the effects of benzodiazepines at the benzodiazepine receptor.[3,4] It has a short elimination half-life of 54 minutes and a partial reversal of neurological depression has been noted after its use as an antagonist.[5] Its elimination half-life is closest to that of midazolam (1.2–3.8 hours)[6,7] and considerably shorter than that of diazepam.[8] The aim of this study was to assess the efficacy of flumazenil in antagonising the effects of midazolam on psychomotor performance, coordination, short term memory loss, and the subjective feelings of pain and drowsiness. These assessments were carried out immediately after reversal of sedation and again before discharge home.

Methods

Fifty patients of ASA grade 1 or 2, aged between 18 and 76 years, who underwent elective outpatient upper gastrointestinal endoscopy at the Western General Hospital Edinburgh, participated in this prospective, double-blind trial. The patients were allocated randomly into one of two equal groups (flumazenil and placebo). The groups were stratified for sex and all patients gave informed, witnessed consent, in accordance with the Helsinki 2 declaration. The study was approved by the Lothian Health Board ethics of medical research committee. Both groups of patients were familiarised with the test battery and each patient was permitted 30 minutes of practice before baseline recordings were made;[9,10] sedation was then administered. The equipment for the tests described below was transported on a trolley of adjustable height so that an optimum position for performance of the tests could be maintained in all cases. The battery of tests took 20 minutes to complete.

Choice reaction time (CRT). Each test involved 30 responses. Total time, latency and motor time were noted (T,L,M).[9]

Critical flicker fusion frequency (CFF). Ambient light, image size, illumination and viewing distance remained constant. The CFF threshold was assessed with increasing then decreasing flicker frequency, five times in each assessment. CFF and CRT were performed using the Leeds Psychomotor Testing Equipment.[9]

Paired word association. The 27 possible correct responses were made up of three lists of three word pairs. The first list contained pairs which were all related, e.g. father–son, the second set were less closely linked, e.g.

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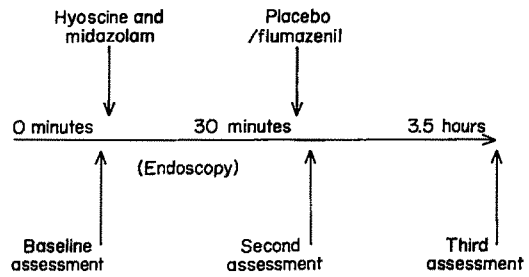

Fig. 1. Sequence of events during study.

scissors–cloth, and the final paired words were unrelated. The patient was familiarised with a new set of paired words for each assessment and was then shown one word of the pair on a television screen and asked to give the other word. Possible responses were correct, incorrect or no response; The first two were noted (paired word association correct, incorrect; PWA,C,I). The maximum possible score was 27.[11]

Wright codoc ataxia meter. This meter is an electronic revolution counter and is attached to the patient at waist level by a bulldog clip on the end of a line. The meter automatically maintains a constant tension on the line and rewinds after the patient sways forwards and backwards. The revolutions of the spindle are counted electronically and the results noted as 'sway'. The units measured are 0.33 of a degree or 20 minutes of arc.[12]

Linear analogue scales. These tests were self-rated and results recorded in millimetres. Sedation and pain were assessed in this way (LSED/LPAIN). These were assessed using scales from 0 (no pain) to 100 (worst pain) and 0 (alert) to 100 (drowsy).

All patients received hyoscine butylbromide 20 mg after the baseline assessment. They were then given a variable dose of midazolam through an indwelling needle intravenously on the dorsum of the hand to produce a level of sedation titrated carefully to point 3 on a five-point scale: 1, fully awake; 2, drowsy; 3, asleep but rousable to command; 4, rousable only to mild stimulation; 5, unrousable. Any patient who could not be roused by command was eliminated from the trial. Thus all patients were sedated to the same end-point and received an equipotent dose of midazolam. The endoscopy was then performed. Thirty minutes later, the patients received either vehicle only or flumazenil 0.5 mg intravenously over 2 minutes. The battery of tests was repeated immediately, and again after 3.5 hours. This time was chosen as the time at which patients were normally deemed fit to return home. The order to be performed was selected randomly on each occasion that the tests were performed. Figure 1 summarises the sequence of events.

The results were analysed using the Mann–Whitney *U*-test for between-group analysis and Wilcoxon Signed-ranks test for within-group analysis.

Table 2. Results at 30 minutes.

	Flumazenil		Control		Two-tailed p
	Mean	SD	Mean	SD	
CRTT	1104.3	745.2	1847.3	1205.5	0.00001
CRTL	715.4	676.5	1131.2	725.3	0.00001
CRTM	396.7	129.6	712.7	544.8	0.0003
CFF	26.2	2.7	25.2	3.9	0.354
PWAC	18.0	3.6	10.6	6.8	0.0001
PWAI	5.1	2.1	8.7	5.8	0.0613
SWAY	46.0	31.0	90.9	63.8	0.0023
LPAIN	17.1	21.4	21.8	23.8	0.4574
LSED	46.2	27.2	65.5	28.0	0.0113

Choice reaction time total, latency and motor (milliseconds); CRT, T, L, M. Critical flicker fusion frequency (Hz); CFF. Paired word association, correct and incorrect; PWAC, I. Wright codoc ataxia meter; SWAY (1 unit = 20 minutes of arc). Linear analogue scale pain/sedation (mm); LPAIN/LSED.

Table 3. Results at 3.5 hours.

	Flumazenil		Control		Two-tailed p
	Mean	SD	Mean	SD	
CRTT	876.9	209.6	888.0	232.1	0.8234
CRTL	532.2	147.0	528.8	139.1	0.7859
CRTM	349.7	96.4	367.6	165.5	0.6908
CFF	26.4	3.0	30.3	13.3	0.0594
PWAC	22.0	3.1	21.4	4.5	0.8453
PWAI	3.2	2.4	3.7	3.3	0.7767
SWAY	18.9	9.7	22.1	20.4	0.7707
LPAIN	17.2	20.3	14.0	22.4	0.364
LSED	30.9	26.7	50.2	18.6	0.0072

Abbreviations as above.

Results

Both groups were well matched for demographic data and total dose of midazolam administered (Table 1).

All patients received hyoscine butylbromide 20 mg (to relax the gastrointestinal smooth muscle) immediately before the injection of midazolam. Only one patient, in the control group, received local anaesthetic spray (lignocaine 60 mg). Her results were analysed along with the others in that group.

Analysis of baseline tests revealed no differences between groups. Between-group analysis for all variables demonstrated that patients in the flumazenil group were significantly better at most of the tests in the battery than were the control group at 30 minutes (Table 2). CRTT in the control group (1847 milliseconds) was long and demon-

Table 1. Demographic data.

	Flumazenil			Control		
	Mean	SD	Range	Mean	SD	Range
Age (years)	53.8	13.8	20–76	50.8	17.3	22–75
Height (cm)	167.3	8.1	153–186	165.6	8.0	152–183
Weight (kg)	67.2	8.9	52–85	69.2	12.4	50–105
Dose of midazolam (mg)	8.8	1.3	6–10	8.6	1.3	5–10

Table 4. Within-group analysis, baseline and 3.5 hours.

	Flumazenil				Placebo			
	Time 0.0 hours		Time 3.5 hours		Time 0.0 hours		Time 3.5 hours	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
CRTT	765.1	160.8	876.9	209.7	801.5	239.0	888.0	232.1
CRTL	468.5	111.2	532.2	147.0	467.8	109.7	528.2	139.1
CRTM	296.2	74.5	349.7	96.4	328.0	143.5	367.6	165.4
CFF	28.7	2.5	26.4	3.0	28.8	3.0	30.3	13.3
PWAC	23.2	4.9	22.0	3.1	24.5	2.3	21.4	4.5
PWAI	2.2	4.9	3.2	2.4	1.2	1.1	3.7	3.3
SWAY	16.3	8.6	18.9	9.7	16.1	8.8	22.2	20.4
LPAIN	19.4	24.1	17.2	20.3	24.1	10.6	16.3	22.5
LSED	21.8	21.5	30.9	26.7	24.1	22.1	50.2	18.6

Abbreviations as in Table 2.

strated significant impairment. Similarly the mean value for 'sway' in the control group (90.9) was high, and three patients in the control group required help to prevent a fall. Thus, the control group were compromised (coordination, psychomotor performance and short term memory) 30 minutes after the administration of midazolam and therefore required supervision. However, there was a wide range in the responses to the battery of tests.

Linear analogue scales for pain showed no statistically significant difference between groups at any time. Pain assessment was included since it may have biased the performance of the other psychomotor tests. The only test that differentiated between the groups at 3.5 hours was the linear analogue score for sedation; patients in the flumazenil group were subjectively more alert than those in the placebo group (Table 3).

Analysis of results within groups and between times 30 minutes and 3.5 hours demonstrated that neither group deteriorated in performance. Both groups improved in most aspects of performance (with the exception of CFF and LPAIN); patients in the placebo group showed greater improvement than those who had received flumazenil. The self-rated pain score did not change significantly in either group throughout the study period and therefore did not contribute to any of the differences demonstrated.

The results of all tests at 3.5 hours had not reached baseline values in either group (Table 4) despite possible learning of the tests. Learning during the study was minimised by adequate practice before the baseline assessment was made. There was a significant difference between baseline scores and those at 3.5 hours in both placebo and flumazenil groups for CRTT (flumazenil group $p < 0.0004$, placebo group $p < 0.0047$) and PWAC (flumazenil group $p < 0.0186$ and placebo group $p < 0.0006$). Thus, a number of patients had impairment of mental function at 3.5 hours. The other tests failed to demonstrate a significant difference.

Discussion

Outpatient clinical investigations under intravenous sedation are undertaken with increasing frequency in older and less fit patients. The recovery facilities in many units are less than ideal and early recovery of neurological function is desirable. Flumazenil has been shown to antagonise the effects of benzodiazepines in outpatients[13,14] and our study confirms these findings. Flumazenil 0.5 mg resulted in significantly better recovery than placebo, although there was no significant difference in CFF, one of the most sensitive tests for measuring benzodiazepine activity on the central nervous system.[9] Control of the variables that affect CFF (ambient illumination, size of image, viewing distance and pupil size) were standardised by fixing the conditions under which the measurement took place. Unfortunately, random change in the order of the six tests over three sessions does not cancel out order effects. Results from each test were compared with results in the same test at another session, and it would have been better for the order to be retained so that the test was performed under similar conditions on each occasion. The effect of alteration in the order of tests is to add to the variance and mask within-group differences. The flumazenil group reported a significantly greater subjective feeling of alertness, at the time of discharge home, 3.5 hours after sedation. This was not borne out by any of the objective assessments and may have dangerous consequences. A feeling of improved alertness might encourage patients to participate in daily tasks, such as driving, for which they are not fit. Neither group had reached baseline values by the time of discharge and all patients were accompanied home.

It is possible that some of the residual effects of sedation were due to hyoscine butylbromide.

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Inhaled fentanyl as a method of analgesia

M. H. WORSLEY, A. D. MACLEOD, M. J. BRODIE, A. J. ASBURY AND C. CLARK

Summary

A study was undertaken to investigate the use of fentanyl by aerosol for postoperative analgesia. Seven patients had placebo, six received fentanyl 100 μg and seven were given fentanyl 300 μg. A significant improvement in postoperative pain, as assessed by linear visual analogue scale, was achieved in the higher dose group, and in both fentanyl groups the time to alternative analgesia was significantly longer than in the control group. Serum fentanyl levels after inhalation of 100 μg reached a plateau around 0.04 ng/ml and after 300 μg at around 0.1 ng/ml after 15 minutes. Inhaled fentanyl may have a useful analgesic effect despite these low serum levels; this supports the hypothesis that the mode of analgesia from inhaled opioids may be different from that after other routes of administration. There were no adverse effects such as respiratory depression, bronchospasm, nausea or drowsiness.

Key words

Analgesics, narcotic; fentanyl.
Aerosols.

A simple method of analgesia which is rapidly effective with the minimum of complex apparatus would be useful for the postoperative patient and for self administration by those suffering severe pain at home. Such systems were developed with infusion pumps, but their widespread use is limited by cost and complexity. Delivery of drugs by aerosol into the respiratory tract is simple and has become widely accepted for the prophylaxis and treatment of asthma, in migraine and in angina pectoris. Modern nebulisers, using hospital compressed gases, or electrically driven air nebulisers, are capable of reliably producing aerosols of fine particle size which penetrate the bronchial tree and are deposited in airways and alveoli.[1,2] Drug is deposited in sites drained by both the bronchial and pulmonary circulations, and will enter the systemic circulation and reach the brain. There is recent interest in the administration of morphine in this way.[3–5]

Fentanyl is a synthetic narcotic analgesic which is highly lipid soluble, has a rapid onset of action, is potent, does not release histamine, and which, in a single dose, has a short duration of action. It is an effective analgesic agent for pain relief. We have therefore undertaken a pilot study to look at the use of nebulised fentanyl as a method of postoperative analgesia.

Methods

Thirty patients in a single-blind study were randomly allocated to receive a standard volume (6 ml) that contained placebo (0.9% saline), 100 μg or 300 μg fentanyl given by nebuliser. Patients were aged 18–65 years, were ASA 1–2, and undergoing a variety of elective surgical procedures (Table 1). Those with known respiratory or hepatic disease, or who were receiving drugs known to interfere with drug metabolism were not studied. Ten patients were allocated to each group. Ethics committee approval and informed written consent were obtained.

Premedication consisted of morphine and cyclizine. Anaesthesia was induced with thiopentone and maintained with nitrous oxide and halothane in oxygen. Additional analgesia was provided with morphine, and muscle relaxants were used where indicated.

Patients who complained of pain in the recovery room were asked to assess its severity on a 10-cm linear visual analogue (LVA) scale which had been explained the day before. Fentanyl or placebo was then administered in a single-blind fashion via an Acorn II nebuliser driven by compressed oxygen and nebulised to dryness in oxygen at a flow of 8–10 litres/ minute to produce a particle size of 2 μ

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Table 1. Ages, weights and times to nebulisation. Values are expressed as mean (SD).

	Control	Fentanyl 100 μg	Fentanyl 300 μg
Age, years	33.6 (15.8)	37.0 (17.9)	41.3 (15.3)
Weight, kg	66.9 (11.6)	74.8 (13.0)	62.9 (13.1)
Time to nebulisation, minutes	13.0 (2.2)	14.0 (3.0)	14.9 (1.9)
Operations	Cholecystectomy (2) Inguinal hernia Breast lump (2) Varicose veins Gynaecomastia	Cholecystectomy (2) Inguinal hernia (3) Circumcision	Cholecystectomy Vagotomy Inguinal hernia Varicose veins (2) Mastectomy and axillary clearance Breast fistula

or less.[1] Pain was assessed by LVA 5, 15, 30, 60, 120 and 180 minutes later on completion of nebulisation. Patients were instructed to request escape analgesia at any time after the 5-minute assessment if pain relief was inadequate. The time to alternative analgesia, either intravenous morphine in the recovery room or intramuscular morphine after return to the ward, was recorded for each patient. LVA scores for nausea and drowsiness were also completed, and peak expiratory flow (PEF) measured at the above intervals.

Venous blood for the determination of serum fentanyl levels was taken before and at 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, 60, 120 and 180 minutes after completion of nebulisation. Fentanyl concentrations were measured by a sensitive, specific radio-immunoassay with a lower detection limit of 0.02 ng/ml (Fen-RIA-200, Belgium). Coefficients of variation were around 5% for both 'within' and 'between'-assay assessments of precision. Differences between the fentanyl and placebo groups were analysed by the Mann–Whitney *U* test.

Results

Only 20 of the 30 patients completed the study because 10 did not complain of any significant pain while in the recovery room. Thus seven patients had placebo, six were given 100 μg of fentanyl and seven 300 μg. Operations performed in each group are listed in Table 1. There were no differences in the ages, weights or times for nebulisation between the groups (Table 1). One patient, who received 100 μg fentanyl, complained of an itchy nose, but no other adverse effects were noted either by the patients or nursing staff in attendance.

There was no significant difference in nausea or drowsiness scores in either of the fentanyl groups compared to controls. Analgesic effect, expressed as a percentage of the pretreatment LVA score, and time to alternative analgesia in the three groups are shown in Table 2. The reduction in the mean LVA in the fentanyl 300 μg group to 23% was significantly greater than the reduction to 67.7% in the control group; the 95% confidence intervals for this difference were −88 to −9% ($p < 0.05$). The mean time to alternative analgesia was significantly prolonged in both fentanyl groups. The 95% confidence intervals for these differences were 12 to 303 minutes in the fentanyl 100 μg group ($p < 0.05$), and 2 to 591 minutes in the fentanyl 300 μg group ($p < 0.05$).

Figure 1 shows the mean fentanyl concentrations in both groups. After inhalation of 300 μg, a peak of around 0.4 ng/ml was reached and a plateau of around 0.1 ng/ml after 15 minutes. No peak was detected after inhalation of 100 μg and levels plateaued around 0.04 ng/ml. An outlying value at 10 minutes in the 300-μg group, which pulled the mean value upwards has been included in the data, although it is difficult to explain and is probably a rogue value.

Mean peak flow was not significantly different between the three groups (placebo group PEF decrease to 42.6% of pre-operative values; fentanyl 100 μg group to 59.8%; fentanyl 300 μg to 52%). There was no decrease in respiratory rate in any subject.

Discussion

These results suggest that inhalation from a fentanyl aerosol can result in useful analgesic effects despite the low

Table 2. Individual patient data of minimum pain score (LVA) and time to alternative analgesia.

	Minimum pain score (% of pretreatment score)			Time to alternative analgesia (minutes)		
	Placebo	Fentanyl 100 μg	Fentanyl 300 μg	Placebo	Fentanyl 100 μg	Fentanyl 300 μg
	80	36	0	5	50	600
	73	40	100	5	308	7
	30	53	30	60	323	543
	52	55	12	85	17	618
	100	29	7	5	124	190
	100	0	6	9	240	130
	39	—	6	11	—	45
Mean	73	36	23	26	177	305
SD	28	20	35	33	132	271

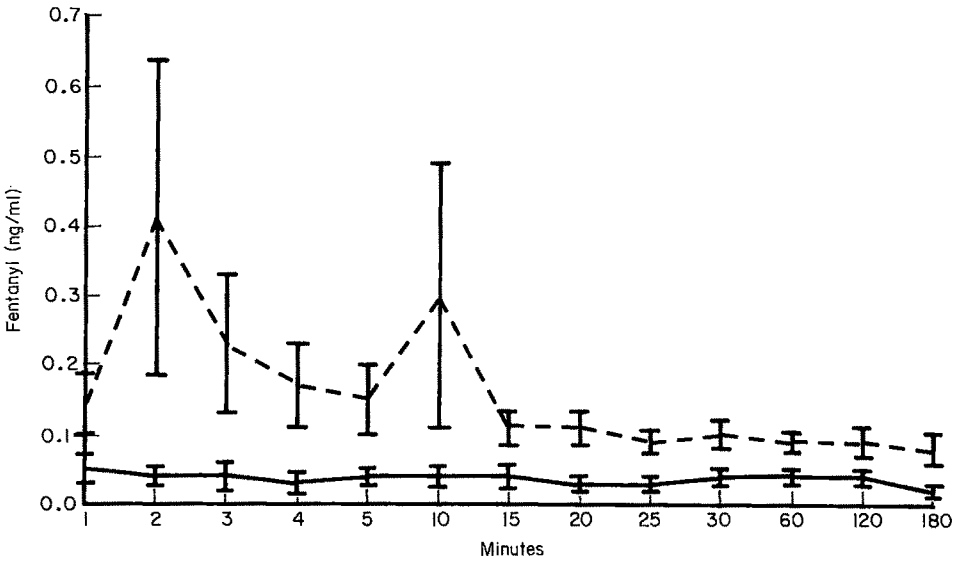

Fig. 1. Mean (SEM) serum fentanyl levels after inhalation. ——, 100μg; – – – –, 300μg.

serum levels obtained. The plateaux of mean serum levels of 0.1 ng/ml and 0.04 ng/ml after the 300 and 100 μg inhalations are lower than the suggested therapeutic threshold of 2 ng/ml in spontaneously breathing subjects.[6] The wide variation in blood levels reflects the unpredictability of fentanyl pharmacokinetics, perhaps due to its lipid solubility and high volume of distribution, which has been noted by other workers.[7]

It has been shown by radiolabelling that approximately 10% of an inhaled dose will reach the lungs and a similar amount may be deposited in the oropharynx. Fifty percent or more may be lost on exhalation and some remains adherent to apparatus tubing.[2,8,9] The serum levels we have recorded would be consistent with the degree of bioavailability to be expected from intravenous administration of a similar fraction of the inhaled dose. Fentanyl is highly potent and might lend itself to administration by dry powder inhalation, which could be equally effective as an aerosol inhalation, but with the potential advantage of convenience and reduced drug wastage from a metered dose inhaler.[10,11]

A useful analgesic effect was demonstrated despite low blood levels; the time to alternative analgesia was prolonged significantly in both fentanyl groups. All but two in each group required no further analgesia for 2 hours, while in the control group all patients required analgesia by this time, and indeed five of the seven needed further doses within 15 minutes. Analgesic effect as assessed by linear analogue pain score was significantly better in the 300-μg group compared with the others. The effect of morphine premedication could explain to some extent the disproportionate analgesic effect gained by the low fentanyl levels. This cannot, however, account for the improved reduction in pain scores from pretreatment values, and the prolonged times to alternative analgesia, since the morphine was given to both treated subjects and controls. It may be that the mode of action of inhaled opioids differs from that after other routes of administration.[4,5]

The results of this pilot study suggest that inhaled fentanyl is an effective, safe and convenient method of analgesia which merits further investigation into such areas as mode of action and methods of administration.

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Variables of patient-controlled analgesia. 3: test of an infusion-demand system using alfentanil

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Summary

Patient-controlled infusion-demand analgesia was studied using alfentanil. We were unable to identify an optimal dose and administration rate; doses required range from 100 to 900 μg alfentanil. The mean concentration of alfentanil in blood associated with return of pain (i.e. immediately before demand) was 58 ng/ml on day 1 and 37 ng/ml on day 2. This difference was despite similar drug consumption on both days.

Key words

Pain; postoperative.
Analgesics, narcotic; alfentanil.

Return of pain is required to prompt further self-administration of analgesic in patient-controlled analgesia (PCA) and therefore an opioid with short latency of effect is desirable with this technique.[1] The low tissue solubility of alfentanil promotes its rapid onset and contributes to its short duration of action.[2] However, demand frequency was unacceptably high in one study of PCA using alfentanil;[3] in another study, alfentanil PCA was supplemented by an infusion system, but the drug was unable to provide relief from severe pain in the very early postoperative period.[4] The duration of analgesia after alfentanil administration is dose-dependent; Lehmann[5] reported satisfactory postoperative analgesia with a mean demand frequency of close to two per hour with a larger demand dose of alfentanil and a low-dose fixed-rate supplementary infusion.

The size of the demand dose in PCA is limited by the adverse effects from the peak plasma concentration after each dose. More drug can be administered with each demand, to result in longer duration of action of each dose yet avoiding toxic peak blood–drug concentrations, when the dose is administered as a brief infusion instead of a bolus. In addition, the inherent safety of pure PCA over hybrid PCA (i.e. with a mandatory infusion) is retained. Infusion demands in PCA, whilst theoretically attractive, were not tested and this study was undertaken primarily to investigate the technique with a variety of dosage regimens. The relationship between pain control and concentration of alfentanil in blood was also examined at the same time.

Methods

The study was approved by the hospital's human ethics committee and all patients gave written informed consent. Consecutive patients scheduled to undergo upper abdominal surgery and aged 18 to 70 years, who were ASA 1 or 2, not taking any analgesic agents or steroids and with normal liver function, were eligible for inclusion.

Patients were tutored in the use of PCA on the night before surgery. The anaesthetic technique was standardised for all patients. Premedication was with oral diazepam; anaesthesia was induced with a titrated dose of propofol plus 75–100 μg/kg alfentanil. Tracheal intubation was facilitated by atracurium and the lungs were artifically ventilated with 70% N_2O in 30% O_2 to an end-tidal CO_2 of between 4.0 and 4.6 kPa. Anaesthesia was maintained with an infusion of alfentanil supplemented with enflurane, titrated between 0.6 and 1.5% inspired concentration. Alfentanil was administered at a rate of 0.75–1.00 μg/kg/minute until 30 minutes before the end of surgery.[6] All patients had surgery performed through an upper abdo-

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Table 1. Numbers of patients by group who received satisfactory analgesia, or reason for withdrawal from the study.

Group	Dose (μg)/ duration (minutes)	Lockout (minutes)	Reason withdrawn				Row total number/ percentage
			Completed study	Inadequate analgesia	Respiratory depression	sedation	
1	60/bolus	3	0	3	0	0	3/ 8.1
2	200/5	5	1	4	0	0	5/13.5
3	300/10	5	2	4	0	0	6/16.2
4	400/12	5	3	7	0	0	10/27
5	300/5	5	1	3	1	0	5/13.5
6	400/10	5	1	2	1	0	4/10.8
7	600/15	5	1	1	1	1	4/10.8
Column total	Number/ percent		9/24.2	24/64.9	3/8.1	1/2.7	37/100

minal incision. Residual neuromuscular blockade was antagonised by neostigmine administered with atropine at the end of surgery. The patient was transferred to the recovery room when spontaneous ventilation was adequate, assessed by respiratory rate, volume and end-tidal CO_2 and started on PCA from a Graseby PCAS (Graseby Medical, Watford, UK). The alfentanil PCA was infused in parallel with the maintenance intravenous fluids through a Life-Med anti-reflux system (Bio-Spectrum, Sydney, Australia). A cannula was inserted in a vein in the contralateral arm to obtain blood samples for determination of alfentanil concentration.

Initially, patients were randomly allocated to receive one of four demand doses of alfentanil (group 1, 60 μg bolus; group 2, 200 μg over 5 minutes; group 3, 300 μg over 10 minutes; 4, 400 μg over 15 minutes). Initial results prompted the addition of three more groups (group 5, 300 μg over 5 minutes; group 6, 400 μg over 10 minutes; group 7, 600 μg over 15 minutes). The lockout interval was 3 minutes after a bolus dose and 5 minutes after all infusion demands.

Patients were studied for the first 24 hours after surgery. Residual pain was measured hourly on a 20-cm visual linear analogue 'slide rule'.[7] The rate of infusion was increased progressively or the dose increased if pain persisted despite administration of two demand doses. Sedation, assessed using a 5-point scale,[8] and respiratory frequency were each recorded hourly. The amount of self-administered alfentanil and the number of valid and early demands (during infusion or lockout interval) made were recorded after 24 hours.

The time integrals of the pain (pain AUC) and sedation scores (sedation AUC) were calculated by the trapezoidal rule for each patient. PCA was stopped if analgesia was inadequate for 2 consecutive hours (pain score above 8 cm) or if the respiratory frequency was less than 8 per minute. No further subjects were allocated to that group when a particular dose of alfentanil was found to be inadequate for three patients.

One nurse observer collected all blood samples. Patients were asked, when the nurse was present, to indicate when additional analgesic agent was required so that a blood sample could be obtained immediately before a demand. The blood–drug concentration at this time was designated the maximum concentration still associated with pain (MCP). The blood was stored in lithium heparin tubes frozen at −30°C before subsequent batch assay. The assay was based on a solvent extraction before gas liquid chromatography with nitrogen phosphorus detection as previously reported for fentanyl.[9] Verapamil was used as the internal standard and the extracting solvent was n-heptane:isoamyl alcohol (98:2). Blood–alfentanil concentrations were determined from freshly constructed calibration curves over the range 0–200 ng/ml. The assay coefficient of variation was 3.9% over this range. Statistical significance of the change in blood–alfentanil concentration from day 1 to day 2 was determined by the Wilcoxon matched-pairs signed-ranks test.

Results

The patients' mean age was 48 years (SD 14) and mean weight was 73 kg (SD 13) with even distribution throughout the groups. The mean duration of anaesthesia was 101 minutes (SD 27). Patients recovered from anaesthesia rapidly (mean time to opening eyes was 7 minutes), and all were quickly able to control their intake of analgesic agent by PCA.

None of the dosing schedules studied were reliably satisfactory and only nine of the 37 patients entered did not require a dose change; the commonest reason for change was poor pain control (Table 1). Increasing the rate of alfentanil infusion after a demand produced good pain control in a further 16 patients so that PCA was continued. The doses required by those patients to achieve good pain control, i.e. dose at end of therapy, are shown in Table 2. There was no correlation between demand-dose size and sedation.

The mean number of valid (good) demands made was 51

Table 2. Dose of alfentanil required to provide satisfactory analgesia.

Demand dose (μg)	Duration of administration of dose			
	Bolus	5 minutes	10 minutes	15 minutes
100	1	—	—	—
200	—	1	—	—
300	—	2	2	—
400	2	2	2	3
500	—	—	—	—
600	—	2	1	1
700	—	—	—	—
800	—	3	—	2
900	—	1	—	—

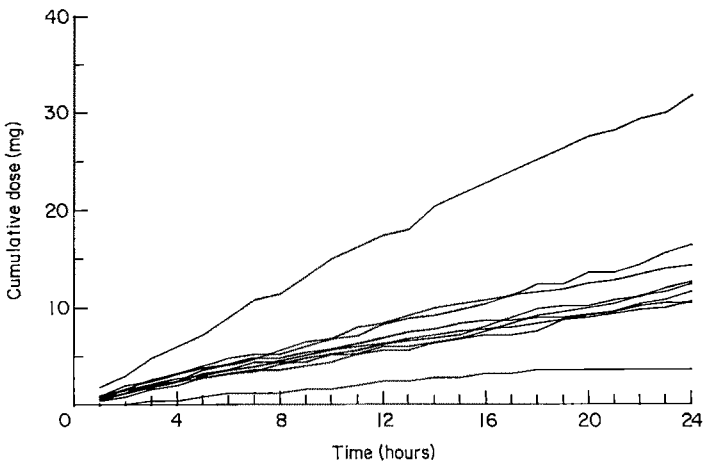

Fig. 1. Cumulative self-administered alfentanil dose for the nine patients who obtained satisfactory pain relief without a change in demand dose.

(SD 27) with a range from 3 to 122 over 24 hours and the mean of total demands was 86 (SD 47) with a range from 9 to 186. The majority of early demands were made during administration of the demand dose rather than in the actual lockout interval. Thus the number of demands made reflected adequacy of control both in terms of pain relief from a particular demand dose and also its speed of onset. The total dose of alfentanil self-administered by patients over the 24 hours ranged from 3.6 mg to 43.2 mg. The cumulative analgesic consumption for each patient is shown in Figures 1 and 2.

Respiratory depression was seen in three patients and occurred after the first or second demand (Table 1). The respiratory rate in these patients slowed within minutes of delivery of the dose although all could be encouraged to increase their ventilatory frequency. Depression of ventilation remote from administration of alfentanil was not seen. Multiple blood–alfentanil concentration data for the first 24 hours were available for 23 patients. The concentration of alfentanil in blood just before patients made demands (MCP) ranged from 21 ng/ml up to 101 ng/ml. The mean MCP was significantly lower (two-tailed $p = 0.006$) on day 2 (37 ng/ml, SD 24), than day 1 (58 ng/ml, SD 25). The mean within-patient coefficient of variation of MCP was 39% (range 3% to 87%).

Discussion

We have been unable to demonstrate, in this investigation, a reliable prescription for pain control from alfentanil by PCA using this range of infusion demands. We had hoped that this technique would have provided pain relief from a small number of demands, but this was not the case. Onset of analgesia was often too slow with an infusion demand, even with alfentanil, and led to a large number of early demands by patients and dissatisfaction with the method. By shortening the duration of administration, that is by providing a more rapid rate of infusion, better pain control was attained. The alternative approach, to increase the dose for a given rate of infusion, was considered, but a trend to an increased incidence of respiratory depression became apparent. It may be that a better dosing profile would be an exponentially decreasing infusion rate that would produce a rapid increase in blood–drug concentration with a more gradual decrease.[10]

There is expected to be a range of demand doses for each

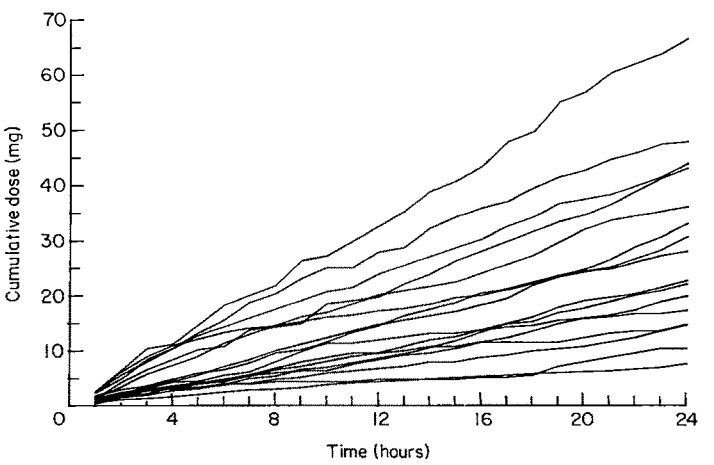

Fig. 2. Cumulative self-administered alfentanil dose for the 16 patients who required a change of demand dose.

analgesic agent that will generally permit good pain control.[11] It has been reported that a 60-μg bolus of alfentanil is satisfactory; we were unable to confirm this. In this study when a demand dose was shown to be too small it was increased, stepwise, until adequate. The demand doses at end of therapy (Table 2) suggest larger demand doses are necessary regardless of the maximum dose obtainable from the PCA apparatus; doses more in line with those used by Lehmann[5] were successful. We were, however, unable to identify a particular demand-dose size that would be appropriate for the majority of patients.

Several patients were withdrawn from the study because of inadequate pain control. This was because the pain scores dictated withdrawal from the study before the demand dose had been increased enough to be effective in that patient. One patient did not derive any benefit from bolus doses of 900 μg alfentanil and had to be withdrawn because this was the maximum demand dose available from the PCA device.

There was no correlation between dose of self-administered drug and sedation; this confirms our impression of lack of sedation during pain therapy with alfentanil, and may be an advantage in using this agent for pain control. The respiratory consequences of alfentanil administration continued after surgery have been reported.[12] The rates of alfentanil self-administration in this study and resultant blood–drug concentrations would not be expected to produce significant respiratory depression nor was it seen.

The minimum effective blood–drug concentration for postoperative analgesia (MEAC) from alfentanil has been reported as over 10 ng/ml.[13] We have measured, in this study, the maximum blood–drug concentration still associated with pain (MCP). Clearly, for such agents where blood–drug concentration-response curves are steep, the two values will be similar. If the aim of drug administration, for example by fixed-rate continuous intravenous administration, is to abolish pain then the MEAC is the appropriate target concentration, but if a concurrent infusion is to be used with PCA then the MCP should be the target concentration so that the patient will still be required to make some demands. Clearance of alfentanil is reduced in the elderly[14] and it should be noted that some drugs often prescribed by surgeons, for instance cimetidine and erythromycin, slow the metabolism of alfentanil and may produce a higher blood–alfentanil concentration than expected from a particular rate of infusion of the drug.[15,16]

The plasma concentration associated with the return of pain is reasonably consistent within the individual when alfentanil is used in a PCA system. The interpatient variability is, however, much greater with a fivefold range in MCP. Also, the MCP appears to decrease with time. It is unclear from the data available whether between day 1 and day 2 there is a gradual decrease or a step-change in the concentration of alfentanil required in blood to relieve postoperative pain. The lower blood–drug concentration was unexpected because the rate of drug consumption on days 1 and 2 (Figs 1 and 2) is similar. The rate of consumption appears so consistent that the dose of alfentanil required over 24 hours might be predicted from the first few hours of PCA use.

This wide range in alfentanil dose requirements has also been described for other opioids used for pain control[17] and is a reason for preferring PCA to fixed-rate continuous-infusion analgesia. There is, however, a minimum alfentanil blood concentration below which few observations fell: an infusion of alfentanil to maintain this concentration (we suggest 30–40 ng/ml) might be a useful addition to PCA with alfentanil. We are currently testing this hypothesis.

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Anaesthesia, 1990, Volume 45, pages 456–457

CASE REPORT

Guillain–Barré syndrome mimicking brainstem death

N. R. COAD AND A. J. BYRNE

Summary

There must be a defined, predisposing condition to fulfil the criteria of brainstem death in the UK. A patient presented recently in coma and with absent brainstem reflexes, but no diagnosis was initially obvious. A subsequent diagnosis of Guillain–Barré syndrome was made, and the patient made a full recovery.

Key words

Brain; brainstem function tests.
Nerve; neuropathy.

A 43-year-old man was admitted recently to our intensive care unit from another hospital where he had been admitted after a 10-day history of an influenza-like illness, and a 4-day history of diplopia, and weakness in the arms and legs. The weakness had progressed rapidly after admission and the onset of respiratory failure necessitated the use of artificial ventilation. He was transferred to our intensive care unit when it was noticed that his pupils were dilated and unresponsive to light. The differential diagnosis, made by the consultant physician at the referring hospital, included Guillain–Barré syndrome and brainstem death. On arrival, brainstem function tests were performed as part of a full neurological examination. The absence of pupillary response to light was confirmed, and testing by a consultant from the intensive care unit revealed absent corneal reflexes, absent vestibulo-ocular reflexes after the injection of 20 ml of iced water into each external auditory meatus (having first confirmed that both tympanic membranes were visible), no response to a suction catheter passed down the trachea, and no response to painful stimuli anywhere on the face. The patient was then disconnected from the ventilator for 10 minutes with oxygen delivered at 6 litres/minute through a suction catheter passed through the tracheal tube. No respiratory movements were observed despite an increase in $Paco_2$ from 5.2 to 7.9 kPa. The patient's temperature was 36.5°C, the urea and electrolyte concentrations were normal, blood glucose was 7.8 mmol/litre and the acid-base status was normal. No hypnotic drugs had been received by the patient for 48 hours. Tests indicated the absence of all brainstem reflexes but in view of the fact that no diagnosis had been made it was decided to carry out further diagnostic tests whilst continuing full care. Computerised tomography and magnetic resonance imaging of the brain were both normal. An electroencephalogram (EEG) showed a normal α rhythm which was unusually dominant and unresponsive to stimulation, suggestive of a brainstem lesion. The protein concentration in cerebrospinal fluid was high (2 g/litre; normal < 0.4) with normal cell numbers. All other results, including a full toxicology screen and tests for porphyria and Wernicke's encephalopathy, were normal. A provisional diagnosis of Guillain–Barré syndrome was made because of the patient's presenting history and the high CSF protein concentration, and full active treatment was continued. There was no change in the patient's condition for the next few days, but it was noticed on day 5 that his pupils reacted to light. A repeat EEG performed at this time showed a marked arousal pattern. It was decided that sedation should be started and that all staff should treat the patient as if he was aware of his surroundings. The patient continued to show very slow signs of recovery over the next few weeks, first regaining movement of his eyes, followed by facial grimacing and shoulder movements. This period was complicated by signs of autonomic instability, with periods of hypertension alternating with hypotension and marked fluctuations in heart rate. These were treated as appropriate. He began to make weak respiratory efforts 15 weeks after his admission, and at the time of writing he has been weaned from mechanical ventilation, and is able to communicate with staff and relatives.

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Discussion

This patient was deeply comatose with absent brainstem reflexes on arrival at our hospital. No sedative drugs had been administered during the previous 48 hours, and metabolic and endocrine causes of coma had been excluded. However, he did not fully satisfy the accepted UK criteria for the diagnosis of brain death,[1] which includes the statement: 'There should be no doubt that the patient's condition is due to irremedial structural brain damage. The diagnosis of a disorder that can lead to brain death should have been fully established.'

The diagnosis of Guillain–Barré syndrome was subsequently made as a result of the presenting history and the raised CSF protein concentrations.[2,3] Such a severe presentation of Guillain–Barré is extremely rare, because although cranial nerve involvement occurs in up to 52% of cases,[4] this usually involves only the facial and bulbar nerves.[5] Involvement of the trigeminal nerves occurs in only 9% of cases.[4] Involvement of the optic nerve and the nerves supplying the external ocular muscles is very rare, and occurred in only one patient in a large study of over 900 cases.[4] However, involvement of these nerves was described as part of the original syndrome by Guillain in 1938.

This patient has recovered progressively and is expected to return eventually to a normal existence. This case emphasises that in order to make the diagnosis of brainstem death, rigid adherence to the guidelines recommended by the Conference of the Royal Colleges and their Faculties (UK)[1] must be observed if mistakes are not to be made and if public confidence is to be maintained in a system which is the basis of requests for organ donation.

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CASE REPORT

Internal jugular catheterisation

Case report of a potentially fatal hazard

H. POWELL AND A. P. G. BEECHEY

Summary

A case is presented of acute life-threatening haemorrhage caused by laceration of the subclavian artery as a result of attempted cannulation of the internal jugular vein. This sequence of events has not been reported previously, and probably resulted from use of a cannula-over-needle system.

Key words

Veins; jugular, cannulation.
Complications; haemorrhage.

Percutaneous catheterisation of central veins has become common procedure in the management and monitoring of severely ill patients. The incidence of complications is higher after cannulation of the subclavian vein than the internal jugular[1–3] and the latter route is used more commonly. We report a case of near fatal acute haemorrhage after accidental laceration of the subclavian artery during internal jugular catheterisation.

Case history

A 56-year-old man with severe triple vessel coronary artery disease presented for bypass graft surgery. Premedication was with oral lorazepam 2.5 mg 2 hours before surgery followed by papaveretum 15 mg and hyoscine 0.3 mg intramuscularly one hour later. The patient arrived in the anaesthetic room breathing oxygen at 4 litres/minute via an MC mask. Peripheral venous and radial arterial lines were inserted under local anaesthesia before induction of general anaesthesia. Anaesthesia was induced and the patient was positioned in a 15° head down tilt for cannulation of the right internal jugular vein using the high technique described by Boulanger *et al.*[4] Two 14-gauge Wallace flexi-hub cannulae were inserted easily and venous blood was aspirated freely. A third cannula was introduced a little lower at the apex of the triangle formed by the sternal and clavicular heads of the sternomastoid muscle. The 'vessel' was located easily 2–3 cm deep to the skin but blood was noted to be a brighter colour compared with the previous cannulations. Blood could be aspirated easily with a syringe, but there was no pulsatile flow. Consequently, the cannula was advanced cautiously over the needle. However, resistance was encountered after insertion by 1–2 cm and the cannulation attempt was stopped, the needle and cannula withdrawn and firm finger pressure applied over the puncture site.

There was a rapid decrease in systolic arterial pressure from 120 mmHg to 50 mmHg and a subsequent decrease to 30 mmHg. This was thought at first to be due to acute left ventricular over-distension caused by the head down position and the operating table was levelled. Calcium and adrenaline were given without effect. External cardiac massage was applied and the patient was transferred to theatre for immediate sternotomy and institution of cardiopulmonary bypass. There was a massive right haemothorax, although there was no obvious bleeding point. The arterial pressure was restored quickly with rapid infusion of blood and colloid solution before cardiopulmonary bypass. The electrocardiogram showed no changes suggestive of ischaemia during the hypotensive period, and the pupils remained small.

Initially, the surgeons were unable to locate the source of haemorrhage and proceeded with the coronary artery surgery. This was completed uneventfully and then the great vessels on the right side were explored. The right subclavian artery was found to be lacerated at its origin from the brachiocephalic artery. The subclavian artery was disconnected from the internal carotid and then re-anastomosed. The total length of the operation was 11.5 hours. The right arm remained warm and pink throughout, and after the anastomosis there was a palpable brachial pulse.

There was considerable drainage of blood from the chest

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drains in the early postoperative period, but this settled over 4 days. A total of 38 units of blood, 24 units of fresh frozen plasma, 20 units of platelets, 10 units of cryoprecipitate and 4 units of human albumin solution was required. There was some initial weakness in the right arm; this improved gradually and normal power was present after 8 days when the patient was discharged from the Intensive Care Unit. He was discharged to convalescence in good health after a protracted stay on the ward.

Discussion

Catheterisation of the central veins is a valuable technique for measurement of central venous pressure, for administration of potent cardiovascular drugs, irritant drugs or parenteral nutrition, and for rapid large volume infusion. Various approaches have been used but the internal jugular route has been found to be the safest,[1-3] although numerous problems can still occur.[5] We have been unable to find any previous reports of acute life-threatening arterial haemorrhage. This is a particularly serious complication: if it had occurred outside a cardiothoracic centre, the patient would probably have died.

In this case, serious damage to the vessel may have been caused by the cannula-over-needle method of insertion. The cannula was probably the cause of the tear in the vessel wall, although the cannula was advanced over the needle with care, and no undue force was applied. The needle of this system is 5 mm longer than the cannula, and other cannula-over-needle systems are similar. It is likely that the needle pierced the outer wall of the vessel and then lodged in the intima so that blood could be aspirated but did not flow freely. The cannula probably pierced only the outer wall of the vessel and then caused an extensive laceration as it was pushed down over the needle.

This hazard would probably have been avoided by using a Seldinger[6] technique for the cannulation. This technique is known to be safer[1,7] but the cannulation sets are more expensive. The additional cost of this patient's treatment was estimated to exceed £5000. In addition, there were 'knock-on' effects from deferred operations as a result of his long stay in the operating theatre and intensive care unit. The additional cost of the use of a Seldinger multilumen central venous catheter compared with our multiple cannulation technique is about £7. Multilumen catheters may be considered more appropriate when several ports of access to the central circulation are necessary since only a single puncture of the vein with a relatively small needle is required for insertion. In addition, there is no risk of shearing off a cannula already situated in the vessel, which could happen when multiple catheters are inserted. However, multilumen cannulae are not suitable for rapid large volume infusion.

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Anaesthesia, 1990, Volume 45, pages 460–461

CASE REPORT

Painful onset of intrathecal blockade

M. S. READ AND D. J. DYE

Summary

A case is described in which a woman with well controlled epilepsy and minor abnormalities of peripheral nerve function in the lower limbs experienced intense pain during the onset of a spinal anaesthetic for operation on burns on her thighs. Possible mechanisms and treatments are discussed.

Key words

Anaesthetic techniques; spinal.
Pain.

Case history

A 54-year-old woman who weighed 98.6 kg was admitted to a tertiary referral Burns unit with infected scalds of her upper thighs and pubic region. She had a long-standing history of epilepsy and of severe osteoarthritis. She was taking anticonvulsant medication and had not suffered an epileptic fit for 15 years. The combination of obesity and osteoarthritis had severely limited her mobility, and she was unable to prevent the burns when, 3 days previously, she had spilled freshly made coffee into her lap.

She had undergone excision of a benign cerebral tumour 10 years previously. Specific questioning and examination showed that her cardiovascular and pulmonary systems were normal. Examination of her nervous system was not performed in detail on admission. There was pronounced swelling and valgus deformity of both knees. She was taking phenytoin 100 mg, primidone 250 mg and diazepam 5 mg, each three times a day and did not drink alcohol or smoke.

Treatment with systemic antibiotics and dressings to the lesions reduced the local cellulitis. Prophylaxis against deep venous thrombosis was provided by low-dose heparin therapy. She was scheduled for surgical debridement and autologous skin grafting of her thigh burns 3 weeks after admission. The burns were no longer painful and her weight had increased to 100.8 kg. Review of the laboratory investigations revealed that she had a mild neutrophilia and a serum alkaline phosphatase of 159 IU/litre.

Premedication was with oral diazepam 10 mg; she was brought to the anaesthetic room where she appeared comfortable and relaxed. An infusion of normal saline was set up using an 18-G cannula in the left forearm. The patient was helped to turn to a left lateral position, and, using a paramedian approach, a 22-G spinal needle was introduced with some difficulty into the theca. Hyperbaric 0.5% bupivacaine 2.25 ml was injected slowly, and the patient was turned back into a supine position. There was sensory blockade up to the level of the umbilicus and weakness of the legs after about 3 minutes, and the patient was taken into theatre. She started, at this point, to complain of an intense pain throughout the entire area of both lower limbs. This was treated symptomatically by the induction of general anaesthesia with 120 mg propofol. The patient was given 50 μg fentanyl, and maintenance of anaesthesia was with nitrous oxide and enflurane via a Mapleson A system and a mask.

Surgery was allowed to proceed. The patient was allowed to regain consciousness after approximately 15 minutes, when harvesting of skin was complete, and with some more propofol immediately available. She confirmed that she was comfortable, that she was unaware of the surgery which was still being performed, and that the pain that she had felt in her legs was no longer present. The remainder of the operation proceeded uneventfully, and the conduction blockade was not noted to last an unusually long or short time.

Examination of the peripheral nervous function in the

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Table 1. Results of neurological examination of the lower limbs.

General	Obese. Crippled with osteoarthritis. Limited mobility
Tone	Normal
Power	Normal
Coordination	Unable to assess due to immobility
Sensation	
Light touch	Hyperaesthesia left calf, otherwise normal
Sharp/blunt discrimination	Reduced on lateral border left foot and on left calf
Vibration	Normal at the wrist. Reduced bilaterally at iliac crests, knees, and ankles. Absent on medial surface of left ankle. Normal in the left hallux. Reduced in the right hallux
Temperature	Normal
Position	Normal in thumbs, absent in toes
Reflexes	
Knee jerks	Absent
Ankle jerks	Absent
Plantar response	Upgoing, bilaterally

lower limbs was carried out after the operation. This revealed minor deficits of sensation and reflexes as shown in Table 1.

Discussion

Painless phantom limb sensations are common during spinal conduction anaesthesia, be it intrathecal[1,2] or epidural.[2] Painful phantom during spinal conduction anaesthesia has been reported in a patient with tabes dorsalis,[3] one with sciatica,[4] one who had suffered previous major trauma,[5] and on numerous occasions in lower-limb amputees.[4, 6–8]

Severe exacerbation of phantom-limb pain may occur during the onset of the block, and it may continue throughout the procedure, or it may disappear in conjunction with an increase in the upper level of anaesthesia as the block develops. One report describes the successful initiation of a low block by the epidural route, and then the appearance of phantom-limb pain when a second injection of local anaesthetic caused an increase in the upper level of anaesthesia.[5]

A theory was proposed that explains some of these phenomena.[9] It is widely accepted that transmission of pain occurs via two pathways, fast Aδ fibres and slower C fibres and that there is modulation of the latter by the former and by nonpain sensory Aβ fibres. The C fibres run with the sympathetic afferents and it is possible that they can ascend a variable distance within the sympathetic chain to enter the spinal cord higher than the level of the associated Aβ and Aδ fibres (and higher than a low spinal blockade), the so-called paraspinal pathway of sensory input. Thus, rarely, an otherwise perfect block may fail to prevent pain from a thigh tourniquet. Blockade of the A fibres may reduce the inhibition of transmission of impulses via C fibres, and unmask previously unfelt pain, in the presence of abnormal sensory pathways or activity (from which the patient may or may not have symptoms). It may be that our patient had some abnormality of sensory function, either secondary to her peripheral neuropathy, or in association with chronic inflammation and disruption of her arthritic knees. One can speculate that the neuropathy was secondary to a folate deficiency state caused by the anticonvulsant medication (this is under investigation), or that there was chronic subclinical trauma to the peripheral nerves as they passed the knees.

It has been suggested that the most effective treatment in this situation is a subanaesthetic dose of thiopentone. This is more effective than morphine, fentanyl, pethidine or diazepam.[8] This finding is particularly relevant in view of the use of subanaesthetic doses of thiopentone as a diagnostic test in the subclassification of deafferentation and central pain syndromes.[10] This was not attempted in this case, but it must be borne in mind that the fact that the pain was no longer present when the patient was allowed to recover consciousness may have been as a result of the residual effect of the anaesthetic drugs.

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Anaesthesia, 1990, Volume 45, pages 462–464

CASE REPORT

Epidural anaesthesia and Von Willebrand's disease

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Summary

A case is described of a primiparous patient with Von Willebrand's type 1 disease and diabetes who presented at 36 weeks' gestation for Caesarean section. This was performed under epidural anaesthesia in the absence of any coagulation disorder. The effects of pregnancy on coagulation factors in this disorder are discussed.

Key words

Anaesthetic technique, regional; epidural.
Complications; Von Willebrand's disease.

Epidural and subarachnoid anaesthesia are contraindicated in the presence of a coagulation defect, because an epidural haematoma may develop if a blood vessel is punctured inside the spinal canal and cause permanent neurological damage.[1] Von Willebrand's disease is a familial bleeding disorder which is associated with either a deficiency of one of the factor VIII protein complexes or an abnormal variant. The two main forms of the disease are described as type 1 with a quantitative deficiency of the Von Willebrand factor and type 2 with a qualitative defect. The mild form (type 1) has an autosomal dominant inheritance.

In normal pregnancy factor VIII increases and so bleeding problems can be expected to diminish. It has been suggested[2] that epidural anaesthesia is feasible for elective Caesarean section if a coagulation screen is normal and therapy is planned in a woman with mild Von Willebrand's disease. We describe the management of such a patient.

Case history

A 41-year-old patient who had been treated for primary infertility became pregnant after *in-vitro* fertilisation. She required a Caesarean section at 36 weeks because of intrauterine growth retardation. This was probably a consequence of her insulin-dependent diabetes, which had been treated since she was 17 years of age. Her insulin requirements had more than doubled during the pregnancy, but she carefully controlled her blood glucose level by repeated sampling and was closely monitored by the physicians.

The diagnosis of Von Willebrand's disease had been made after she bled after an operation on her hand when she was 24 years old, and she was treated with factor VIII. She received an infusion of 1-deamino-8-p-arginine vasopressin (DDAVP) when she was presented for laparoscopy in the *in-vitro* fertilisation programme and the response is shown in Table 1. Similar results followed DDAVP therapy for an egg collection and laparoscopy, but after the latter procedure bleeding occurred into the abdominal wall and cryoprecipitate was given. DDAVP was administered again at 15 weeks' gestation for a diagnostic amniocentesis. There was a progressive improvement in her Von Willebrand's disease during her pregnancy and the results of her haematological investigations are recorded in Table 1.

The patient requested an epidural for Caesarean section. The only abnormal finding was ankle swelling on physical examination. The local and general complications of epidural anaesthesia were discussed with the patient and her husband. Four units of blood were cross matched and factor VIII and cryoprecipitate were available if required. She received ranitidine 150 mg the night before surgery and a further 150 mg ranitidine orally 2 hours before operation. Oral metoclopramide (10 mg) was administered an hour before surgery and 30 ml 0.3 M sodium citrate immediately before she arrived in the operating theatre. An infusion of 5% dextrose was commenced and Actrapid insulin (1 unit/ml) administered by a syringe pump to maintain a blood glucose level of 4.5–6.0 mmol/litre. A separate large bore cannula was inserted for fluid replacement. A lumbar

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Table 1. Haematological investigations performed in the pregnant and nonpregnant state.

	Factor VIIIC %*	VWF %**	Ristocetin cofactor %***	Bleeding time (minutes)	Prothrombin time (seconds)	Activated partial thromboplastin time (seconds)
Normal values	50–150	50–200	50–200	<6	13–17	21–37
Nonpregnant March 1988						
Pre DDAVP	42	30	—	>15	16	36
Post DDAVP						
0.5 hour	155	58	—	5	—	—
2 hours	101	80	—	—	—	—
5 hours	84	62	—	—	—	—
22 hours	55	38	—	—	—	—
May 1988						
After cryoprecipitate	—	151	22	—	17	30
Pregnant 15 weeks						
Post DDAVP						
0.5 hour	109	26	17	7.3	—	—
2 hours	131	56	31	—	—	—
23 weeks	86	35	8	6.5	—	—
36 weeks	108	—	10	6	14	30

*Measured using a modified APPT method with standardised plasma; **quantitative measure of antigen by ELISA; ***qualitative method using platelet aggregation methods.

epidural catheter was sited using loss of resistance to saline through a 16-gauge Tuohy needle at the $L_{3/4}$ interspace. No blood or cerebrospinal fluid was obtained. Bupivacaine 0.5% in divided doses was injected into the epidural space to a total of 28 ml and a block from T_5 to S_5 was established. She was tilted to the left and the baseline blood pressure of 130/80 mmHg was maintained by the infusion of 2 litres of crystalloid solution. The heart rate, electrocardiogram and oxygen saturation were monitored continuously and the blood pressure measured at 3-minute intervals. Oxygen was given by mask and the operation was allowed to proceed.

Delivery was difficult because the baby was in a breech position with extended legs, but a female infant was delivered which had an Apgar score of 9 at 1 and 5 minutes. Intravenous oxytocin (10 IU) was administered after delivery and a bradycardia developed with a blood pressure of 100/80 mmHg and she felt nauseated. Atropine was given, but the upper abdominal discomfort continued, so papaveretum was given intravenously in 2-mg increments until she was comfortable. Blood loss during surgery was estimated to be 450 ml. The epidural catheter was removed intact at the end of surgery.

The patient developed a wound haematoma which spontaneously ruptured and she had an episode of hypoglycaemia after operation. There were no sequelae related to the epidural.

Discussion

Von Willebrand's disease is the commonest of all inherited haemostatic disorders; the incidence of overt disease is about 1 in 10 000, similar to haemophilia A, but subclinical forms of the disorder are common. Von Willebrand's disease has an autosomal inheritance, in contrast to haemophilia, an X-linked disorder, and therefore is the most frequent genetic haemostatic disorder in obstetric practice.[3] It is a disorder which can present in forms of different severity and pathology, so opinions have been divided as to whether or not obstetric epidurals are contraindicated in this condition. A conservative view is that the condition *per se* is a contraindication to epidural analgesia in obstetrics.[4] Other recommendations relate the condition to its presentation at the time of delivery. In the present case report, where elective surgery was scheduled with adequate investigations which were normal and preventive therapy available, the request of the patient was considered to be a reasonable one. The choice of a regional technique could then be made between an epidural or spinal block. Subarachnoid anaesthesia with a 25- to 29-gauge needle may be indicated because the small needle is less likely to injure a blood vessel. It was not chosen in this case because the history of intra-uterine growth retardation suggested that there may be placental insufficiency, and a technique of divided doses of bupivacaine given into the epidural space was considered less likely to reduce cardiac output and hence placental blood flow.

Fibrinolytic activity is suppressed and clotting factors increase, especially fibrinogen, by the end of the first trimester of pregnancy which results in a hypercoagulable state. This continues until delivery of the placenta when normal fibrinolytic activity rapidly occurs. The factor VIII complex, which is a component of the intrinsic pathway increases significantly during the second and third trimesters. The two main parts of factor VIII consist of a procoagulant factor VIIIC (deficient in haemophilia) which is linked by noncovalent bonds to a larger multimeric molecule called Von Willebrand's factor (VIIIWF). This latter molecule can be deficient (type 1) or abnormal (type 2) in Von Willebrand's disease. The VIIIWF forms the largest proportion of the factor VIII complex, and increases in pregnancy by about 375% and factor VIIIC by 200%. The multimeric structure of the Von Willebrand's factor was normal at the end of pregnancy in type 1, but in type 2 abnormal patterns are still present and a return to normal coagulation cannot be expected in this type of disease.[6]

The Von Willebrand factor appears to stabilise the small coagulant protein VIIIC, or perhaps protect it from proteolytic digestion. Reduction in VIIIF usually leads to

comparable reduction in VIIIC activity. Clinical manifestations are primarily those of a platelet defect, namely spontaneous mucous membrane and skin bleeding with prolonged bleeding after trauma or surgery. There is in addition a variable secondary defect of factor VIIIC activity which, if severely depressed, may lead to manifestations of a coagulation disorder.

The function of the factor VIII complex can be estimated by measuring the bleeding time and platelet adhesion or platelet aggregation in the presence of the antibiotic ristocetin. The bleeding time and ristocetin cofactor are useful in assessing the severity of the disease,[7] but even when the bleeding time is increased and the ristocetin cofactor is reduced, bleeding may not be a hazard if factor VIIIC is adequate or borderline. The second trimester results of the patient described in this case report show a reduced ristocetin cofactor, a slightly prolonged bleeding time, a reduction in the Von Willebrand factor and a normal factor VIIIC. The prothrombin time and activated partial thromboplastin time, screening tests of the extrinsic and intrinsic coagulation pathways, were normal at the time scheduled for her delivery. The two investigations which had changed markedly from the nonpregnant state were the factor VIIIC level, from 42 to 108%, and the bleeding time, from more than 15 minutes to 6 minutes.

The use of an infusion of 1-deamino-8-p-arginine vasopressin is an established method of managing type 1 Von Willebrand's disease for surgical procedures. It was administered in this case before a laparoscopy and then for amniocentesis. The increase of plasma factor VIII and Von Willebrand's factor is rapid but transient, as demonstrated in the patient's haematological results (Table 1), so that an increase in synthesis of these factors is unlikely to account for its effect. The infusion is well tolerated, unlike other drugs which are known to increase factor VIII, but it can increase the heart rate and cause mild facial flushing,[8] probably related to its peptide structure, so the patient was closely monitored during its administration. These effects are reduced by increasing the duration of the infusion. DDAVP also has antidiuretic properties since it is a synthetic analogue of the antidiuretic hormone 8-arginine vasopressin, but a water overload of the patient can be avoided. DDAVP is a useful alternative to blood products which could cause post-transfusion hepatitis and it can be used in pregnancy.[9] However, the bleeding time is not substantially shortened by DDAVP and the individual response is variable.[10]

In mild type 1 disease, where the Von Willebrand factor in the nonpregnant state is normal but deficient, the stimulation of the production of coagulation factors during pregnancy can produce a normal coagulation picture and bleeding time.[9] This was demonstrated in this case report. The patient returns to the prepregnant state once delivery of the baby occurs and coagulation problems can present. It is for this reason that the epidural catheter was removed as soon as possible after delivery. The blood loss at operation was within normal limits but a haematoma developed in her abdominal wall. Mothers with Von Willebrand's disease and a low factor VIII are at risk of postpartum haemorrhage. This would also be a complication of Caesarean section after general anaesthesia, with the problem of avoiding trauma to the airways. There may be a case for administering DDAVP in the puerperium because factor VIIIWF decreases rapidly in Von Willebrand's disease once the uterus is empty.

The choice of epidural anaesthesia for Caesarean section in the presence of a known coagulopathy requires the anaesthetist to be familiar with the natural progression of the disease and its treatment, and especially to elicit the assistance of a haematologist in the initial investigation and management. A more disconcerting problem arises when a patient is presented for epidural anaesthesia and the anaesthetist is unaware of the presence of a coagulopathy,[9] either because of inadequate investigation or knowledge of drug therapy. An adequate history is essential, especially with regard to familial disorders and drug ingestion; when managing patients with different presentations of Von Willebrand's disease one must be aware that the mild form is likely to cause more postpartum than intrapartum problems.

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APPARATUS

The Fenem CO_2 detector device

An apparatus to prevent unnoticed oesophageal intubation

W. T. DENMAN, M. HAYES, D. HIGGINS AND D. J. WILKINSON

Summary

A new oesophageal intubation detector device, the Fenem CO_2 detector, was used in 100 patients intubated during anaesthesia for elective surgery. This new device was 100% accurate in the differentiation between tracheal and oesophageal placement of a tube.

Key words

Carbon dioxide; detection.
Intubation; tracheal.

There is a need for a reliable and simple aid to confirm correct tracheal intubation. The results of unnoticed oesophageal intubations are catastrophic and yet these events still occur.[1] We rely at the moment on a variety of tests and manoeuvres to confirm the placement of our tubes but these have not solved the problem. A recent review by Birmingham *et al.*[2] has highlighted this situation which remains a cause of concern for all anaesthetists at some time in their careers. We tested a device which was portable, reliable and simple to use and which indicated the presence of carbon dioxide in exhaled gases.

Detector device

The device tested was the Fenem CO_2 detector (Fig. 1).[3–5] It is a small, portable plastic attachment which is inserted into the breathing system between the tube and catheter mount. The detector weighs less than 30 g and has an internal volume of 38 ml. It offers minimal resistance to flow (less than 0.3 kPa at 60 litres/minute) and can be attached to the catheter mount before intubation, and thus does not delay connexion of the breathing system to the tracheal tube.

The dome of the device is clear plastic with a coloured membrane visible which is normally purple. This is stated to indicate that less than 0.3% carbon dioxide is present. If carbon dioxide is present the membrane changes to yellow on exhalation and on subsequent inspiration the colour returns to purple. A colour coding is printed around the outside of the dome to provide a reference. Rapid detection of placement of the tube and breath-by-breath monitoring is possible.[4]

Methods

One hundred ASA 1 or 2 patients were included in the study and all were admitted for elective surgery and required tracheal intubation as part of their anaesthetic sequence. None had evidence of ischaemic heart disease or hiatus hernia and there were no detectable signs of oral, pharyngeal, laryngeal, tracheal or oesophageal abnormalities in any patient investigated, as assessed at the visit before operation.

The patients were anaesthetised by one of the four authors in a manner appropriate to clinical needs. Premedication was at the anaesthetist's preference. Three methods of tracheal intubation were used. Those who were to receive suxamethonium were given oxygen before intravenous induction of anaesthesia. Patients to be paralysed with a non-depolarising agent were given an intravenous induction and then their lungs were manually ventilated with 50% nitrous oxide in oxygen with an added inhalational agent. Every patient had full monitoring as recommended by the Association of Anaesthetists[6] and where available, pulse oximetry was included. Spontaneous ventilation continued throughout intubation in those patients intubated with a blind nasal technique.

Intubation was performed once anaesthesia had been induced and the patient prepared as described above. Intubations were undertaken by doctors of various grades and by students, but were supervised by an anaesthetist. The detector was attached within the gas delivery system and the position of the tube determined, once the tracheal tube had been placed. Any misplaced tubes were immediately resited. Correctly placed tubes were secured and anaesthesia and surgery then continued.

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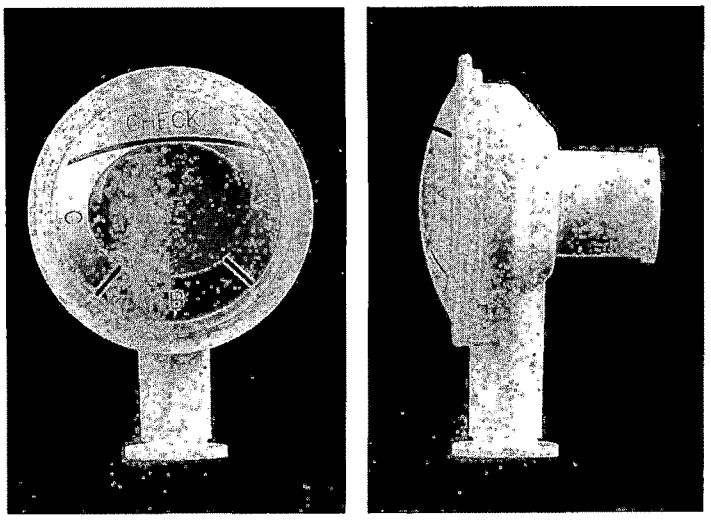

Fig. 1. The Fenem CO_2 detector device.

Results

All patients had uneventful induction and intubation sequences and no clinical evidence of hypoxia was seen in any patient at any time. There were 100 intubations attempted by a variety of theatre personnel: 82 by registrars, 10 by students and 8 by consultants.

Ninety-seven patients had the tube placed in the trachea at the first attempt. Three patients had the tube placed in the oesophagus, but were immediately reintubated correctly. The determination of the placement of all 100 tubes was based on the colour displayed by the Fenem detector. The colour of the device remained purple and indicated absence of carbon dioxide in the exhaled gases in all oesophageal intubations.

Not all those patients in whom the tube was correctly placed were straightforward (vocal cords not seen in 14 patients, chest movements equivocal in one and breath sounds equivocal in one patient). The Fenem detector nevertheless turned a yellow colour, which indicates the presence of more than 2% carbon dioxide in the exhaled gases, in all 97 cases.

Discussion

The indications of correct tube placement are all fallible, as illustrated by the number of different methods used to determine position.[1,2,7-10] The importance of the detection of oesophageal intubation is obvious; the literature is full of accounts of the results of undetected misplacement and the confidential reports into maternal deaths continue to reiterate the results of erroneous intubation. In addition, the courts are beginning to realise what the majority of anaesthetists have believed for a long time, that this mistake is avoidable and consequently medicolegal costs are soaring.[1]

The use of auscultation of breath sounds after intubation has its advocates but this is not always reliable especially in children or in noisy surroundings. Chest movement is another possible indicator of correct tracheal intubation but is fallible in the obese.[8] Many anaesthetists would argue that the only perfect way to be confident about tube position is to visualise the vocal cords at laryngoscopy and watch the tube pass through them. This is not always possible.

Wee[9] and Nunn[10] described methods for detecting oesophageal intubation. The device described by Wee is a 50-ml syringe coupled to a catheter mount. The catheter mount is connected to the tracheal tube and aspiration attempted after intubation. If aspiration is possible then tracheal placement is assumed. This test relies on the different physical properties of the trachea and oesophagus. The pliable wall of the oesophagus is expected to occlude the lumen of the tube, whereas the rigid wall of the trachea allows aspiration. One failure is reported.[11]

Previous studies[2] have shown that detection of carbon dioxide in exhaled gases is probably the best determinate of correct intubation, and while a capnograph is frequently available in theatre it is not at other sites at which intubation occurs. Transfer of patients is associated with tube dislodgement which is unnoticed and might be detected with continuous exhaled carbon dioxide monitoring. We agree with Strunin and Williams[5] that the Fenem detector, unlike a capnograph, needs neither maintenance, nor calibration, nor does it represent a large capital outlay and is therefore of great value.

We believe that the capnograph, when available (and this usually means within the theatre, ICU or casualty department) remains the apparatus of choice to confirm accurate intubation. Until all such sites have these devices the Fenem CO_2 detector will provide vital information to any personnel who attempt tracheal intubation. The Fenem detector has a unique role outside the hospital environment due to its portability and accuracy.

The Fenem CO_2 detectors used in this study changed colour in the presence of carbon dioxide and therefore indicated correct tube placement. The device is easy to use and can be left attached to the patient either throughout the anaesthetic or during any change in position of the patient. It is therefore possible to detect late tube dislodgement should it occur. The manufacturers recommend six breaths be given before a definite decision is made. This is to ensure that no carbon dioxide has been trapped in the stomach after gastric distension during oesophageal ventilation. There have been several reports of carbon dioxide in the stomach, such as the cola complication[12] and the study

by Linko *et al.*[13] However, these problems would also arise if a capnograph were used which is why the minimum of six breaths is a recommended guideline.

We believe that this simple device will prove valuable in all areas of anaesthesia but particularly in obstetric practice, in the accident and emergency department and wherever cardiopulmonary resuscitation is performed.[14]

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HISTORICAL NOTE

Walter Stoeckel (1871–1961)

A pioneer of regional analgesia in obstetrics

A. DOUGHTY

The earliest report of the use of regional anaesthesia for the relief of labour pain was published in 1900 by Oskar Kreis,[1] an assistant obstetrician at the Women's Hospital in Basel. He achieved immediate and total anaesthesia of the lower part of the body in six parturients by the subarachnoid injection of cocaine, but it was at the cost of nausea, vomiting and postpartum headache in all but one of his patients. In 1909, Walter Stoeckel of Marburg described a series of 141 cases of obstetric epidural analgesia[2] in an article entitled 'Über Sakrale Anästhesie'.

Walter Stoeckel was born in 1871, the son of a farmer. He was educated at the grammar school at Insterburg in East Prussia, that small enclave of pre-war Germany on the Baltic coast sandwiched between Poland and Lithuania. Stoeckel was not a bright scholar; he even had to repeat one year's study and he only just scraped through his university entrance examination, but his early personal experience and his later observation of undergraduates led him to believe that performance at school was an unreliable guide as to suitability for higher education. He had intended to qualify as a veterinary surgeon and ultimately to become manager of a stud farm, but his father persuaded him to take up medicine. He studied at Konigsberg in East Prussia and then in Munich and Leipzig.

In his memoirs,[3] he recalls the profound impression made on him when he witnessed childbirth for the first time during his clinical training. He qualified in 1895 and, after compulsory military service and a year as a ship's doctor, he worked for 5 years as an assistant in the gynaecological clinic at Bonn University. In 1904 he became Chief Assistant to Professor Bumm at the Charity Hospital in Berlin and a year later was appointed as honorary professor in Berlin University. After a further 3 years, and much to the surprise of his colleagues, he was simultaneously offered the chairs of gynaecology by no less than three universities, Greifswald, Erlangen and Marburg. He accepted the chair at Marburg, a city 80 km north of Frankfurt; Stoeckel held this post for 3 years and it was here that he carried out his pioneer work on obstetric analgesia.

A special interest in gynaecological urology drew his attention to the therapeutic use of caudal injections described in Paris by Cathelin[4] in 1901. Admittedly Cathelin envisaged relief of labour pain as one of the possible therapeutic applications of the procedure but he never used it for this purpose himself, indeed, as a urologist it was unlikely that he would have had the opportunity; but let Walter Stoeckel himself tell the story. Here is offered an English translation of his historic paper which could have been the foundation of current practice had its implications not been ignored.

'The idea of injecting anaesthetic drugs into the sacral canal stems from the French urologist, Cathelin.[4] His technique was reported in a paper translated by Strauss of Barmen entitled "Epidural injections by sacral canal puncture". Cathelin's hope of finding a method equally effective as, and safer than, spinal anaesthesia has not been fulfilled. The effect of sacral injection is so inferior to spinal anaesthesia that there is no comparison between the two methods for operative surgery. The superiority of Bier's procedure (*i.e. spinal anaesthesia*) must be emphasised without any reservation. Nevertheless, the epidural technique cannot be dismissed as completely useless.

'Cathelin himself first used a solution of 30–40 ml of physiological saline, not as a surgical anaesthetic, but as therapy in various disorders of the urinary tract. In particular he stated that it was effective in a high proportion of adolescents with urinary incontinence. He believed that the injection caused an increased sensitivity of the bladder to normal stimuli and that the pain of cystitis and of urethritis seemed also to be temporarily alleviated. Among German workers, Kapsammer[5] of Vienna reported satisfactory results in the treatment of enuresis. I myself have treated with epidural injections a number of bed-wetters, children and adults of both sexes; the results will be reported elsewhere.

'I have the impression that it is possible to affect the innervation of the pelvic viscera by the direct action of fluid on the nerve plexus within the sacral canal. Because of the close relationship between the innervation of the bladder and the uterus, it occurred to me to use the method for gynaecology and midwifery and to find out if the sensitivity of the uterus could be affected by an epidural injection. As I felt certain that the pain of labour was due to the uterine contractions, I decided to make use of Cathelin's epidural injections during parturition. By this means it might be possible to achieve the ideal of painless childbirth by a temporary interruption of the nerve pathways carrying labour pain, thus avoiding the need for a general anaes-

Footnote The italics in the translation of Stoeckel's paper are the author's interpolations.

Based on a paper read to the History of Anaesthesia Society in February 1989. Andrew Doughty, FFARCS, FRCOG.
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thetic. Cathelin had not used this application of his technique, but he had warned of the danger of cocaine intoxication particularly in late pregnancy: but now we have in Novocaine an excellent and safe substitute for cocaine and as I know that we can safely undertake spinal novocaine injections, I could see no danger in using it for epidural injections. I therefore injected into the sacral canal of a primigravida in the expulsive stage of delivery, 3 ml of the same novocaine–adrenaline solution that we use for spinal anaesthesia. The result exceeded my expectation. (*Here it is difficult not to suspect an inadvertent subarachnoid injection.*) The labour pains vanished, while the progress of labour remained unimpaired. The birth of the child followed so painlessly that the mother was totally unaware of it. Inspired by this initial success, I decided to abandon the scopolamine–morphine combination then in use in my clinic and to test sacral anaesthesia further; but before reporting on my results up to the present I must briefly review the anatomy and technique of the method.

'The anatomy of the sacral canal has been well demonstrated by Cathelin and I would recommend reading of his work to anyone interested. (*Then follows a short description of the bony landmarks and contents of the sacral canal.*)

'It is clear that there are important differences between the spinal and sacral methods both as to the site of injection and to the spread of the injected solution. With spinal anaesthesia, the fluid injected into the subarachnoid space can spread within the meninges right up into the cranium, but with Cathelin's method the spinal cord and meninges remain inviolate as the fluid spreads between the dura and the periosteum of the vertebral canal. It always remains outside the dura and is therefore "epidural", or more accurately, "extradural".

'I have attempted to demonstrate in a cadaver the height attained by sacral injections in the epidural space. Methylene blue was found to spread up the vertebral canal sometimes up to the lower thoracic region. The solution also flowed along the course of the sacral nerves through the sacral foramina into the retroperitoneal connective tissue of the posterior pelvic wall, but on one side only.

'I do not wish to extrapolate the results of postmortem experiments to living patients. Live tissues are able to absorb and hold injected fluids. How far the fluid spreads upwards and laterally from the sacral canal must depend on the quantity and fat content of the connective tissue and on the volume of injection. Cathelin's view that fluid cannot possibly track along the sacral nerve roots because of a dense connective tissue block in the foramina, I do not consider to be adequately substantiated.

'As regards technique, I have followed Cathelin's directions. The patient lies on the left side. Knees and thighs are fully flexed, the latter being pulled up against the abdominal wall. In the lateral posture the line of the sacral vertebral spines is not contiguous with the natal cleft, so the sacral hiatus lies above the apparent mid-line. This knowledge is particularly important for the accurate identification of the bony landmarks. The right hand inserts the needle through the sacrococcygeal membrane; there is little difficulty in finding the correct path with absolute certainty but in advancing the needle one must avoid impinging upon the periosteum of the anterior or posterior wall of the sacral canal. After piercing the sacrococcygeal membrane, the direction of the needle must be altered by gradual depression of its hub. The needle, when correctly sited, lies almost immobile. The injection should be given slowly. If the skin over the hiatus swells at the first push of the plunger of the syringe, it is a certain sign of incorrect placement of the needle as the fluid is being deposited subcutaneously; the needle must then be withdrawn and correctly re-inserted. Pain is caused either by an inordinately rapid injection or by the incorrect siting of the needle.

'The solution injected was physiological saline mixed with varying percentages of novocaine with or without adrenaline. The most effective mixture proved to be 30–35 ml of 0.5% Novocaine with 1 in 300 000 adrenaline. The management of the various changes of volume and composition of the fluid injected and the observation of its effect was made possible only with the close cooperation of my assistants, Drs Bierhoff, Mayer, Esch, Heinrichsdorf and Sieber to whom I am grateful for their support and for their helpful suggestions for modification of technique during the research.

'In this work we tried to remain objective; we did not wish to be so impressed by good results as to be blinded to unwelcome side effects and complications. It was not always easy to maintain this resolve. The intellectual level of women delivered in our hospital is sometimes low or at least inadequate to enable us to decide on the quality of the pain relief achieved by the injection. One must guard against biased suggestions and avoid asking leading questions of the mother so that she gives the desired answer solely to be rid of the importunate interrogator. We observed 141 cases, 89 primigravidae and 52 multiparae. The injection was used only in normal pregnancies and we excluded all women in whom a complication was recognised or suspected. Usually only one injection was given but in two cases a second injection was given after a lapse of time. Ninety-six patients received the injection during the first stage and 45 in the second stage of labour.

'Effect on labour pain

In 18 cases there was no noticeable beneficial effect and in a further 12 the relief of pain was minimal. Positive relief was obtained in the remaining 111 cases but to varying degrees. It became apparent that labour pain is not a single entity but is made up of two distinct components which became recognisable by our experience with sacral anaesthesia. A nonanaesthetised mother usually states that the pains in the lower back are the most severe and they radiate forward like a belt. When the head has passed the pelvic brim the site of the pain changes as a result of the stretching of the perineum. After an effective sacral block the pain of uterine contraction disappears or at least diminishes and becomes quite tolerable. Women often state that, instead of back pain, that which is now perceived over the pubic symphysis amounts only to a very minor discomfort. Of course, the woman has now become aware of it after the injection because it had previously been masked by the very much more severe back pain. We have obtained complete relief or reduction to a tolerable degree of the back pain in 72 cases and of both back and hypogastric pain in 39 cases. The considerable degree of relief was evidenced by the behaviour of the mothers in whom the pains were no longer accompanied by loud crying and rolling about in bed; the contractions could then only be perceived by abdominal palpation. Many mothers with

previous experience of labour stated that there was no doubt as to the difference between the present birth aided by sacral anaesthesia as compared with other confinements.

'Pain sensitivity in the perineum was mostly, but not always, obtunded when tested with a needle. Thus the passage of the head through the vulva was painless in nine cases and only very slightly painful in 16. Three women were delivered by forceps and two had perineal tears sutured quite painlessly. In two other cases, sacral anaesthesia was insufficient for the application of forceps and these patients had to be helped with a few drops of chloroform. In many cases there was a marked relaxation of the pelvic floor musculature.

The onset of the effect of the injection was usually after 3–5 minutes; its duration was very variable, between a few minutes and 6 hours. The average duration of pain relief was 1 to 1.5 hours.

'Effect on uterine contractions

Any method of pain relief that interferes with the progress of labour is unacceptable and a danger to both mother and child. This danger exists with several of the established methods of anaesthesia as there is unquestionably a relationship between the strength of the pain and the progress of the labour. Early in labour the mother's pain is due to the uterine contraction but towards the end, the pain is of perineal pressure and stretching of the vulva. This is the afferent stimulus for the bearing-down reflex; the stronger the pain the more strongly does the mother bear down. It is difficult to determine whether the experience of pain has a similar role in the progress of the first stage but it is possible that complete abolition of pain could well adversely affect the whole progress of labour. For this reason, we watched the uterine contractions very carefully after the sacral injection. In 23 cases the contractions became weaker and less frequent and this depressive effect was especially noticeable if the injection had been given too early in labour; in one case the contractions ceased with the pain and did not return for 4 days. This suggested to us that perhaps a threatened abortion or a premature labour could be suppressed by sacral anaesthesia, but unfortunately the opportunity to test this hypothesis has not arisen. However, if labour had been well established, neither the uterine contractions nor the expulsive forces were affected as a general rule; but in a few cases where perineal sensitivity had been greatly reduced, the bearing down effort was diminished—a striking proof of its reflex dependence on vulval stretching. In four cases we ended labour with forceps because of undue delay in the delivery of the head; in one of these fetal bradycardia was a clear indication but in the other three a spontaneous delivery could well have been achieved.

'In the post-delivery period we had a few cases of uterine hypotonia; we blamed this on the sacral injection, perhaps unjustly, for in 141 deliveries, a few cases of hypotonia must be expected fortuitously; but we justified our assumption for the sake of scientific integrity. However, since we added adrenaline to the injected solution there were no further cases of uterine hypotonia. Since using adrenaline the blood loss at delivery was markedly reduced. Of the 141 cases, 100 lost under 500 ml, 33 lost 500–1000 ml, six lost 1000–1500 ml and only two lost over 1500 ml.

'Side effects and complications

There was little evidence of harm to the fetus. In only three cases was there slowing of the fetal heart rate but the infants were delivered in good condition without any sign of asphyxia.

'It was particularly gratifying that no case of urinary retention was seen in the puerperium so none required catherisation. This is not easy to reconcile with the known therapeutic effect of epidural injections in enuretics. The condition of the mothers in the puerperium confirmed our view that, in general, sacral anaesthesia is a method completely without danger and without coincident or subsequent ill effects. Nevertheless our confidence was shaken by the following case of an infected injection.

'The woman had complained of pain during the injection and, as labour pain had not been relieved, more local anaesthetic solution was injected. It was then realised that the total dose of 60 ml must have been given through an incorrectly sited needle although there was no obvious reason for this suspicion. During the puerperium an abscess appeared in the right gluteal region requiring a large incision. Quite clearly, the tip of the needle had been inserted under the periosteum of the posterior wall of the sacral canal as a few small flakes of necrotic bone were discharged during the granulation and healing of the wound. Bacteriological tests on the solution of Novocaine–adrenaline solution supplied by the pharmacy showed the presence of streptococci and the same organism was isolated from the pus discharged from the abscess. This was certainly a double error—a gross lapse of asepsis and a technical fault, the latter excusable, the former not.

'Conclusions

In summary I would particularly like to stress that, on the results so far, I am not recommending sacral anaesthesia as an ideal procedure. I have tried it out because it seemed logically well-founded and because it offered a new approach to the problem of the relief of pain in labour. I have drawn attention to the shortcomings of the method in its present form and I readily admit that equal or more profound effects are obtainable by general anaesthesia, by scopolamine–morphine or by the spinal anaesthesia recently used by us. On the other hand I doubt whether any of these methods are as safe as sacral anaesthesia. They cause constant anxiety to the doctor, they affect the woman's well-being to a greater or lesser extent and they add side-effects which mar their clinical application. With sacral anaesthesia the pain relief, generally speaking, is not so complete, but the mother shows no sign of stress. She remains conscious, she is neither cyanosed nor restless, her central nervous system is totally unaffected, she shows no sign of shock and has no post-partum headache. In short, she buys her freedom from discomfort cheaply and is not a source of anxiety to her doctor.'

Comment

So ends this translation of Walter Stoeckel's paper published in 1909. Now, 80 years on, what can we say of this man who discovered and appreciated the potential of regional obstetric analgesia years before other pioneers in the field? It is surprising that he did not persevere in

developing his discovery. He stayed in Marburg for only 3 years; perhaps it was only there that conditions were ideally suited to his research. He moved on to Kiel and then in 1925 he succeeded his former professor in the prestigious chair at the University of Berlin. There he busied himself with the creation of ideal working conditions in his clinic, constantly stressing the importance of keeping pace with modern developments and insisting on the provision of the necessary equipment and facilities. He became the leading German gynaecologist of his time, establishing a world-wide reputation in the treatment of uterine cancer. His particular interest was in gynaecological urology, in fact he held strong views that *all* urology in women should be managed by the gynaecologist. He wrote a book on cystoscopy and published a massive text-book of gynaecology which ran to 14 editions. For many years he was editor of *Zentralblatt für Gynäkologie*, the journal in which his paper on sacral anaesthesia had appeared in 1909.[2] From his department emerged no fewer than 20 professors of gynaecology and 34 heads of other gynaecological departments.

Something of Stoeckel's character may be discerned from his paper on sacral anaesthesia. Here was no autocratic professor taking for himself alone the credit for work done in his department. He readily acknowledges his debt to Cathelin and others for developing the technique of sacral injection and he mentions the help received from his juniors, naming them individually. Despite his humane compassion for the sufferings of mothers in labour, he displayed also a mature scientific detachment, refusing to be dazzled by the drama of his discovery. He recorded his observations with honesty, both the successes and the setbacks.

Stoeckel enjoyed a happy family life, retaining to the end a deep interest in current affairs, in horses and a great love of music. He died in 1961 and his memoirs were published 5 years later;[3] it is from these that most of his personal details have been gathered. But the mystery remains: the memoirs give little more information concerning his work on sacral anaesthesia than can be gained from reading his paper published in 1909.

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SPECIAL ARTICLE

Rate-responsive pacemakers and anaesthesia

A consideration of possible implications

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Summary

A new generation of pacemakers has been developed in recent years which adjust the pacing rate according to changes in physiological variables. The selected parameters are affected during physical activity that involves an increased heart rate in healthy humans. The variables include body movements, QT interval, breathing, temperature, myocardial contractility, oxygen saturation and changes in blood pH which may be influenced during general anaesthesia, and can lead to unphysiological, high, pacing rates. It is important to be familiar with the pacemaker and its functions before administration of anaesthesia in order to prevent complications. Rate-responsive pacemakers in such situations should be programmed to exclude the rate-responsive function.

Key words

Equipment; pacemakers.
Complications.

Pacemakers were introduced in the 1960s as valuable tools in the treatment of cardiac conduction defects. Technical development and improved diagnostic possibilities have led to their increased use. They are predominantly implanted in patients who suffer from intolerable bradycardia, which is either caused by sinus node dysfunction, third or second degree atrioventricular (AV) blocks, or who are treated with large doses of drugs which reduce heart rate.[1] However, the emergence of more advanced pacemakers include indications other than bradycardia. Instruments which respond to paroxysmal tachycardias or episodes of ventricular fibrillation have been developed.[2]

Rate-responsive pacemakers are implanted in patients with indications similar to those who require normal pacemakers (VVI or AAI). (For pacemaker terminology, See Table 1). Basically, those that are rate-responsive eliminate bradycardia in the same way as do other pacemakers, by securing a basic heart rate, which is individually programmed, usually between 50 and 80 beats/minute for adults. However, the rate-responsive pacemaker can stimulate the heart to increase its rate in response to an increased demand, such as physical activity. Patients with the 'normal' fixed, basic-rate pacemaker may experience dyspnoea and fatigue as a result of physical activity, because they cannot improve their cardiac output with an increase in heart rate.[3] There is increased metabolism and increased demand on the cardiopulmonary system during exercise. In addition oxygen consumption and arteriovenous oxygen saturation differences increase. The production of CO_2 and lactate rises, which leads to a decreased pH in mixed venous blood. The generation of heat in the active muscles raises the temperature of mixed venous blood and heart rate, myocardial contractility and ejection fraction increase as a result of a rise in circulating catecholamines; preload and stroke volume also increase. Electrophysically, the Q-T interval is shortened by increases in heart rate and circulating catecholamines.

The variables mentioned above can be used in the algorithms of various rate-responsive pacemakers in order to regulate the pacing rate, so that they correspond to the patient's level of physical activity.[4–6]

At first this new generation of pacemakers were predominantly implanted in younger patients, whose level of physical activity was sufficiently high to be restricted by a fixed, low heart rate. However, since older patients also benefit from this type of pacemaker, an increasing number of physiological (i.e. rate-responsive) pacemakers will be implanted in this group of patients, who will from time to time require general anaesthesia. This paper therefore reviews the different types of rate-adjusting pacemakers

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Table 1. Pacemaker terminology.

Letter 1.	Chamber(s) paced
	A: Atrium
	V: Ventricle
	D: Dual (A & V)
Letter 2.	Chamber(s) sensed
	A: Atrium
	V: Ventricle
	D: Dual (A & V)
	O: Asynchronous, dose not apply
Letter 3.	Response to sensed event
	T: Triggered
	I: Inhibited
	D: Dual (T or I)
	O: None (asynchronous)
	R: Reverse
Letter 4.	Programmability
	P: Programmable (rate and/or output)
	M: Multiprogrammable
	C: Communicating
	O: None
	R: Rate-response
Letter 5.	Special tachyarrhythmia functions
	O: None
	P: Pacing
	S: Shock
	D: Dual (P+S)
	(The NASPE/BPEG generic pacemaker code).

and describes some of the problems that are likely to be encountered during general anaesthesia in patients fitted with these instruments.

Physiological pacemakers

These pacemakers are of two types: those which use electrodes in the atrium and the ventricle (dual chamber) and those that are rate responsive by using physiological variables to adjust the pacing rate.

Dual-chamber pacemakers

Some patients who suffer from cardiac conduction defects have normal sinus node function and normal atrial contraction and in these a pacemaker with double leads may be used. One electrode is placed in the right atrium and senses the P wave and then, according to the P-wave frequency, the right ventricle is paced via the second electrode which is placed in the ventricle. This pacemaker has a variable pacing rate depending on the rate of atrial contraction and the atrial contribution to the filling of the right heart is preserved.[7] This type of pacemaker has been modified in recent years to include both sense and trigger function in the right atrium and right ventricle (DDD).

The dual-chamber pacemaker has a minimum ventricular pacing rate which is triggered if the atrial P-wave frequency is too low or if the pacemaker cannot sense the P-wave, for example in cases of atrial fibrillation. It also has a maximum ventricular pacing rate; if the P-wave frequency is higher than the programmed maximum ventricular stimulation rate, the pacemaker will return to A-V synchrony by establishing a Wenckebach block. The manufacturers have built-in different algorithms for fall back rates if atrial flutter or tachycardia develops.[7] The dual-chamber pacemaker has restricted application because it can only help the 45% of patients with normal sinus node function; sinus node dysfunction is seen in 55% of the patients with bradycardia.[5] For this reason other physiological variables are used to regulate the pacing rate in the rate-responsive (physiological) pacemakers.

Rate-responsive pacemakers

The types of rate responsive pacemakers and the physiological changes to which they respond are shown in Table 2. This field is expanding rapidly and the clinical application of some of these instruments is at the moment still limited.

Movement-sensing pacemakers

Detection of body movements is the most commonly used method in rate-responsive pacemakers. This type (Activitrax 8403/8413, Medtronic and Sensolog 703/2034, Siemens Elema)[6-8] has a piezoelectric crystal (made of barium titanate or lead zirconate), sensitive to very slight movements, built into the pacemaker unit. Physical activity gives off vibrations of between 5 and 40 Hz which stimulate the crystal to generate electrical impulses. These signals are registered and filtered in the electronic circuits of the pacemaker and are used to regulate the pacing rate. They are programmed individually so that a certain increase in activity produces a corresponding rise in the pacing rate. The upper and lower pacing rate limits are programmed.

Both passive and active body movements are sensed by this type of pacemaker; driving in a car on a bumpy road may also produce an increase in pacing rate, but this is mostly well tolerated by the patient. A similar situation may arise during general anaesthesia and an increase in heart rate may result from changing the patient's position or from vigorous surgical manipulations. This is usually of short duration and will not affect the patient's cardiac performance. Postoperative shivering may activate the pacing system if the movement frequencies fall within the frequency-detecting 'window'. Other conditions of regular muscular activity may also induce a paced tachycardia, e.g. epileptic seizures or electroconvulsive therapy. The sensivity of the pacemaker to body movements is individually programmed and usually they must reach a certain magnitude and duration to induce an increase in heart rate. The muscular twitches produced by suxamethonium and the myoclonus resulting from intravenous anaesthetic drugs are unlikely to induce an increase in heart rate. We have previously reported a patient with a rate-responsive pacemaker in whom an increase in heart rate occurred during vigorous surgical manipulation in the course of a Caesarean section.[10]

Q-T sensing pacemakers

The first rate-responsive pacemakers to be implanted in appreciable numbers were the Q-T sensing pacemakers (Quintech TX 911 and Rhythmyx TX 919, Vitatron Medical).[4,6] This instrument is provided with a right ventricular sensing electrode which measures the time interval from the stimulus to the T wave. The duration of the Q-T

Table 2. Types of rate responsive pacemakers and possible anaesthetic hazards.

Pacemaker sensor	Physiological basis	Algorithm of the pacemaker	Pacemaker name	Manufacturer	Approval	Anaesthetic hazard
Activity	Muscle movement	Piezoelectric crystal activation	Activitrax Sensolog	Medtronic Siemens	Clinical Clinical	Vibration of patient or pacemaker
QT interval	QT decreases as heart rate increases	Onset of paced QRS to end of T wave	Quintech TX	Vitatron	Clinical	Drugs interfering with intracardiac conduction time
Respiratory	Respiratory rate	Thorax impedance changes	Biorate	Biotec	Clinical	Ventilation rate
Respiratory	Minute ventilation	Thorax impedance changes	META	Telectronic	Clinical	Hyperventilation
Temperature	Central venous blood temperature	Measurement of temperature changes	Kelvin 500 Nova MR Thermos	Cook Intermedics Biotronik	Clinical Clinical Clinical	Changes in blood temperature
pH	Central venous pH	pH measurement changes			Preclinical	pH changes
dP/dt	Right ventricular pressure	Piezoelectric crystal in the pacing lead	Deltatrax	Medtronic	Clinical	Factors affecting right ventricular pressure
O_2 saturation	Central venous blood saturation	Hemoreflectorimetry	Oxytrax	Medtronic	Clinical	Oxygen treatment
Right ventricular stroke volume		Intraventricular impedance			Preclinical	
Ventricular depolarisation gradient		Integration of paced evoked QRS complex	Prism CL	Telectronics	Clinical	

interval varies according to blood catecholamine levels and heart rate. The Q-T interval is normally between 250 and 400 msec, but the pacing rate is changed according to variations in measured Q-T interval. The change in Q-T period observed during pacing at various rates determines each pacemaker's setting. In this way the pacemaker is programmed to increase or decrease the pacing rate in sympathy with changes in activity, such as during physical exercise.[4,6]

This pacemaker is supposed to behave as programmed during general anaesthesia. However, if drugs which can affect the Q-T interval are administered, the reaction to an increased level of catecholamines may be attenuated. Beta adrenoceptor blockers are reported to decrease the Q-T interval which leads to an attenuated response to physical activity in patients with a Q-T pacemaker.[11] Thus this type of rate-responsive pacemaker may need reprogramming whenever there is a major change in the administration of anti-arrhythmic drugs. In addition to factors that effect the general threshold (pH, potassium level, local anaesthetics), any medication which changes the T-wave configuration may be important since this may interfere with the rate-responsive function.[12,13]

Respiration sensing pacemakers

The respiration-regulated pacemakers have an established relationship between the changes in heart rate and respiration, which occur during exercise (Biorate MB1, Biotec and META 1202, Telectronics).[4,6,14] The electrical impedance of the thorax varies with the lung volume and by measuring this impedance, respiration-regulated pacemakers can register changes in the respiratory frequency and tidal volume (i.e. minute ventilation). There is also an increase in oxygen consumption and CO_2 production with increased physical activity. This induces an increase in pulmonary minute ventilation, which is sensed as changes in thoracic impedance by the pacemaker. The instrument is programmed so that an increase in ventilation will lead to a matched rise in pacing rate.

Special attention should be directed to the degree of ventilation if a patient with this type of physiological pacemaker requires artificial ventilation either in the operating theatre or in the intensive care unit. The pacemaker should be reprogrammed to exclude the rate-responsive function in cases of deliberate hyperventilation.

There may be problems with general anaesthesia if the anaesthetist is not familiar with the function of a respiration-sensing pacemaker. In our department, a patient with a minute ventilation-regulated pacemaker (META 1202, Telectronics) had a transurethral resection of the prostate and his lungs were manually ventilated. Accidental hyperventilation led to a paced tachycardia and a decrease in arterial blood pressure, which was interpreted as a sign of hypovolaemia. However, when the anaesthetist was occupied with setting up a blood transfusion, ventilation was reduced and this led to the pacing rate returning to normal.[15]

Temperature sensing pacemakers

There is initially a slight decrease in blood temperature of about 0.2°C at the start of physical activity, caused by increased venous return of blood from peripheral vessels. Later, during continued activity, blood temperature increases as the blood is warmed in the exercising muscles. Pacemakers with a thermistor built into the pacing electrode can sense the temperature changes in the mixed venous blood (Sensor Kelvin 500, Cook pacemaker Corp.; NOVA MR, Intermedics; and Thermos, Biotronik).[16,17] The decrease in blood temperature at the onset of physical activity triggers the pacemaker to react (with greater sensitivity) to an increase in temperature in mixed venous blood. The pacemaker can detect changes of ± 0.02°C.

There is an equivalent increase in the pacing rate depending on the rise in temperature. The pacemaker has a programmed fixed lower pacing rate, so that hypothermia will not induce a bradycardia.

There is considerable variation in the temperature response to physical activity, which will depend on the patient's general, and especially physical, status. The anaesthetist may also predict problems in relation to rewarming of hypothermic patients. There is usually a temperature decrease of 0.5 to 1.0°C during general anaesthesia which will make the pacemaker more sensitive to any subsequent increase in temperature. The increased sensitivity reduces the pacemaker's reaction time to a change of activity. Small increases in temperature will not raise the paced heart rate if the patient is normothermic at induction of anaesthesia, but later becomes slightly hypothermic. However, if the patient is already slightly hyperthermic, induction of anaesthesia may lower the temperature to normal and then even small increases will induce a rise in paced heart rate. A problem may also appear during rapid infusion of warmed fluids via a central venous catheter, since this will stimulate the pacemaker's sensor to increase the pacing rate.

Myocardial contractility sensing pacemakers

Another type of sensor which has been employed in rate-response pacing is the myocardial contractility (dp/dt) of the right ventricle.[18] Right ventricular pressure is dependent on venous return (preload), outflow resistance (afterload) and myocardial contractility. Intraventricular pressure increases during physical activity, due primarily to an increased preload and circulating catecholamines. This type of pacemaker (Deltatrax, Medtronic) has a pressure transducer incorporated into the pacing electrode which measures changes in the intraventricular pressure. These changes represent various levels of physical activity so the pacemaker can change the pacing rate accordingly. Several factors may contribute to changes in right ventricular pressure during general anaesthesia, such as the patient's position, e.g. head down, positive pressure ventilation, inferior vena cava compression, rapid infusion via a central venous catheter or administrations of sympathomimetic drugs. These changes could induce the pacemaker to stimulate the heart with an unphysiological rate.

Oxygen saturation sensing pacemakers

These pacemakers measure changes of oxygen saturation in mixed venous blood by a photocell placed in the pacing lead (Oxytrax, Medtronic).[19] The basis for this algorithm is an increase in oxygen consumption during exercise which will lead to a diminished oxygen saturation in mixed venous blood; this is sensed by the pacemaker, to result in an increased pacing rate. Oxygen saturation in the mixed venous blood during general anaesthesia may also be affected: metabolism is reduced and oxygen extraction diminished, so oxygen saturation in mixed venous blood will usually be higher than normal provided that there are no problems with arterial oxygenation. The pacemaker will pace at a preset basic heart rate at high oxygen saturations. However, those with acute respiratory insufficiency or with drug-induced respiratory depression may have a low saturation that will stimulate the pacemaker to increase the heart rate. This may further impair the function of a failing heart.

Other types of physiological sensors for rate-responsive pacing

Several other parameters are under investigation as potential sensor systems for rate-responsive pacemakers. Pacemakers that are able to measure pH in mixed venous blood have been developed. The increased metabolism in relation to physical activity raises the production of CO_2 and lactate and lowers pH, which can be used to regulate the pacing rate.[20]

The evaluation of cardiac performance in relation to physical activity has also introduced stroke volume as an algorithm for physiological pacing. The volume of blood in the right ventricle may change from one stroke to another; these changes cause fluctuations in electrical impedance in the ventricles. There is an increase in stroke volume during exercise and consequently an increase in the electrical impedance. This is then used to regulate the pacing rate.[21]

The ventricular depolarisation gradient is an integration of the paced evoked QRS complex. A technique in which the ventricular depolarisation gradient is an electrocardiographic parameter which describes the spatial distribution of activation time associated with ventricular excitation can be used. Physiological conditions which increase sympathetic activity and synchrony of ventricular contraction are manifested as a decrease in activation dispersion. Conversely, conditions associated with a decrease in sympathetic activity are reflected as an increase in activation dispersion. The pacemaker registration of the QRS is similar to the Q-T interval registration used in the QT pacemaker.[22]

Problems may be expected with physiological pacemakers in unusual situations. They are designed to function optimally during periods of rest and exercise. However, the patient may be stimulated in such a way, during surgery or in the intensive care unit, that the pacemaker interprets a significant change of activity and stimulates the heart in an unphysiological manner.

The future trend in the development of rate-responsive pacemakers may incorporate two or more sensor systems in order to improve the pacemaker's reliability.[23] The combination of dual-chamber pacing and muscle movement sensor (Synergyst, Medtronic and Synchrony, Siemens) is already in clinical use.[24,25] A dual-chamber pacemaker with either a breathing sensor (Telectronic) or a temperature sensor (Intermedics) is also being tested.

Discussion

We have mentioned some of the problems which may be experienced by the anaesthetist when rate-responsive pacemaker sensor systems are subjected to changes that occur during anaesthesia and which may result in an unphysiological pacing rate. However, the complications which are described by others concerning the 'normal' types of pacemaker (VVI and AAI) may still be seen. Cases with suppression of demand pacemaker by electrocautery have been described by several authors,[26,27] as have incidences of pacemaker failure in hyperkalemia,[28] hypokalemia,[29] acid-base imbalance[30] and as the result of local anaesthetics.[31] Placement of a magnet over the pacemaker can activate different test programmes, for example threshold values for stimulation/capture (Vario test).[32] However, placing a magnet over a pacemaker during the use of diathermy may cause reprogramming of the pacemaker.[33]

Specific pacemaker complications are usually rare in general anaesthesia. Pacemaker patients often have other ailments besides a cardiac conductance disturbance, which may be far more troublesome from the anaesthetic viewpoint. The introduction of more advanced pacemakers should not present problems to the anaesthetist provided the mode of action of the instrument is fully understood.

Patients with rate-responsive pacemakers are generally very well and even tend to forget that they actually have a pacemaker implanted.[34] They should carry a note to indicate the type and programming of the pacemaker, but it is possible to identify the pacemaker type by X ray. The anaesthetist should aquaint him/herself with the type of pacemaker at the pre-operative visit, and if this is rate responsive, the type of sensor must be familiar to the anaesthetist in order to avoid unphysiological changes in pacing rate during anaesthesia. Depending on the type of operation and the anaesthetic technique to be used further information may be required, either from a pacemaker manual or by consulting a pacemaker specialist. Intraoperatively, most pacemakers (physiological dual-chamber pacemakers will pace with the sinus/atrial frequency) will pace at the basic rate since the patient is supposed to be in a state of rest, although situations may arise where the pacing rate may change, and this may reduce cardiac output and lead to hypotension.[35] The anaesthetist should be aware of this risk and to avoid this situation it may be necessary to exclude the rate-responsive function. This is done with a special programming device which differs for the individual pacemaker type.

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Anaesthesia, 1990, Volume 45, pages 477–480

Forum

A comparison of the effects of alfentanil/droperidol or fentanyl/droperidol on intra-ocular pressure

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Summary

The influence of two intravenous sedative regimens on intra-ocular pressure was investigated in conjunction with retrobulbar local anaesthesia. Forty patients were allocated randomly to either group A (alfentanil and droperidol) or group F (fentanyl and droperidol). Measurements of intra-ocular pressure, arterial pressure and oxygen saturation were made before operation, after premedication, after intravenous sedation and after surgery. $Paco_2$ was also measured before and after operation. Each sedation technique caused a similar reduction in intra-ocular pressure. There was less effect on $Paco_2$ and oxygenation in group A.

Key words

Analgesics, narcotic; fentanyl, alfentanil.
Eye; intra-ocular pressure.

The control of intra-ocular pressure (IOP) during ophthalmic surgery is of prime importance, and the factors which influence IOP have been described.[1] Much published work has involved the use of general anaesthesia,[2,3] but an increasing amount of cataract surgery is performed under local anaesthesia with sedation.

IOP depends on extra-ocular muscle tone, scleral rigidity, and vascularity of the orbit. Marked increases in central venous pressure, for example the Valsalva manoeuvre or hypercapnia that leads to venous engorgement, can increase IOP. Drugs used to produce sedation during cataract surgery under local anaesthesia would be expected to reduce IOP, but the possibility exists that other effects of sedation, such as hypercapnia or hypoxia, may affect the pressure adversely.

The aim of this study was to measure IOP in patients who have cataract surgery performed under local anaesthesia, accompanied by an intravenous sedative technique which has been in routine use in this unit, namely fentanyl and droperidol.[4] Alfentanil has a shorter duration of action than fentanyl[5] and has been shown to produce a greater decrease in IOP compared with fentanyl during general anaesthesia.[6] A fentanyl and droperidol regimen was compared with one of alfentanil and droperidol, since cataract surgery is performed commonly on an elderly population.

Method

The study was approved by the local ethics committee and written informed consent was obtained from each patient. Forty patients who were to undergo elective cataract surgery under local anaesthesia with sedation were recruited. Twenty patients per group represents a sample size with 90% power to detect a difference, based upon a standard deviation of 3.7 mmHg for changes in IOP.[6] Patients of ASA grades 1, 2 and 3, of either sex, over 18 years of age and within the weight range 40–90 kg were eligible for inclusion. Those patients with severe systems impairment, known sensitivity to opioids, Parkinsonism, who took drugs with known extrapyramidal side effects, or with markedly increased IOP, were not studied.

A radial arterial blood sample was taken before operation to determine $Paco_2$. The patients were premedicated at the discretion of the anaesthetist (A.E.M.) with either no premedication or 2, 5 or 10 mg diazepam orally 2 hours before operation. An intravenous cannula was sited in the dorsum of the hand in the anaesthetic room. The patients were allocated randomly to receive intravenous sedation with a solution of either alfentanil 400 μg and droperidol 5 mg (group A) or fentanyl 100 μg and droperidol 5 mg (group F), in each case made up to 10 ml with normal saline. Sedation was administered by the same anaesthetist on each occasion (A.E.M.) and was titrated to patient requirement according to verbal contact, degree of ptosis and observation of degree of sedation.

The local anaesthetic nerve blocks (retrobulbar and facial nerve) were performed by the surgeon, after sedation and before further IOP measurement, using a 50:50 mixture of 0.5% bupivacaine and 2% lignocaine without adrenaline. IOP was measured in the nonoperated eye by the ophthalmic surgeon who was unaware of the nature of the sedation, using a Perkin's hand-held applanation tonometer,[7] after instillation of benoxinate and application of fluoroscein from an impregnated strip to the cornea. An average of three readings was taken at each measurement

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point. Arterial pressure was measured with a semi-automated sphygmomanometer (Copal). Oxygen saturation was measured during the procedure with a Biox 3700 pulse oximeter (Ohmeda), using a finger probe.

IOP, arterial pressure and saturation were measured at the following times: before operation (baseline); in the anaesthetic room; in the operating theatre, after an optimum state of sedation was achieved; and at the conclusion of surgery. The volume (ml) of sedative drug combination used was noted, as well as the time at which it was administered, and any further incremental doses were similarly recorded.

Oxygen 6 litres/minute was administered in the operating theatre, via a specially modified facemask, and the ECG and oxygen saturation were monitored throughout the procedure. Duration of surgery was noted. Intra-arterial blood sampling was repeated at the conclusion of surgery to determine $Paco_2$. The incidence of nausea, vomiting and analgesic requirements were noted at 1 and 12 hours after surgery.

Data were analysed by analysis of variance, and paired and unpaired Student's *t*-tests as appropriate.

Results

One patient in group A was not included for technical reasons, therefore data were available for 19 patients in group A and 20 in group F. There was no significant difference between the groups in terms of age, weight, sex distribution, chronic medication and ASA grading (Table 1) or in baseline measurements of IOP, arterial pressure, $Paco_2$ or oxygen saturation (Table 2).

Eight patients in group A and five in group F received no premedication. The doses of diazepam were distributed similarly between the groups. The initial volume of sedation solution (mean, SD) administered was similar for each group: group A 6.9 (2.0) ml and group F 7.5 (1.8) ml. There was no difference between the groups in the amount or number of increments given (Table 3).

There was a statistically significant within-group difference in IOP when baseline measurements were compared with those taken in the anaesthetic room. In group A, IOP decreased from a mean of 16.7 to 13.5 mmHg ($p < 0.005$), and in group F from 15.8 to 13.1 mmHg ($p < 0.05$, Fig. 1). This decrease did not correlate with the dose of premedication. There was a significant decrease in IOP after sedation to a mean value of 8.0 mmHg in group A and 8.5 mmHg in group F ($p < 0.001$), and this level of IOP was maintained

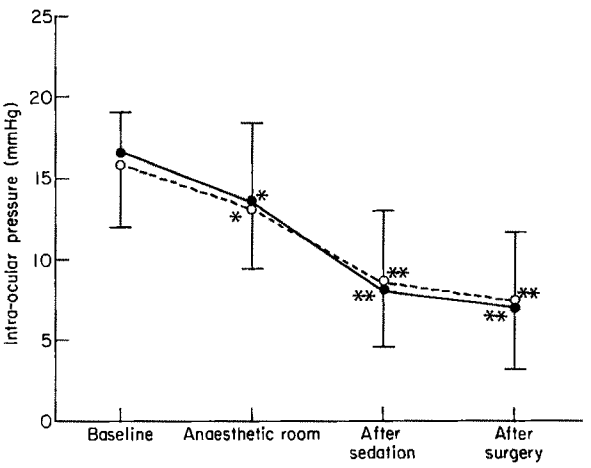

Fig. 1. Intra-ocular pressure (mmHg), mean, SD. Group A, (●—●); Group F, (○---○). *$p < 0.05$ compared with baseline; **$p < 0.001$ compared with anaesthetic room reading (within-group difference).

until the end of the study period. There were no between-group differences.

There were no significant changes in systolic arterial pressure in group A. There was a significant decrease in group F after sedation from a mean (SD) of 155 (26) to 133 (31) mmHg ($p < 0.05$), which recovered to presedation values at the end of surgery (Fig. 2). There were no between-group differences. Pre-operative and postoperative $Paco_2$ did not differ between the groups. However, there was a slight increase in $Paco_2$ in group A from a mean of 5.25 (0.39) to 5.36 (0.48) kPa ($p < 0.05$), and a larger increase in group F from 4.99 (0.45) to 5.41 (0.52) kPa ($p < 0.0001$).

There was a decrease in oxygen saturation in each group after sedation but before administration of supplemental oxygen, from 95% to 92% in group A and from 94% to 90% in group F ($p < 0.001$). The postsedation values (92% compared with 90%) differed significantly between the groups ($p < 0.05$, Fig. 3). The increase in oxygen saturation after administration of oxygen was similar in both groups.

The mean (SD) operating time was similar in each group, 28 (8) minutes in group A and 30 (8) minutes in group F, but the overall time from sedation to end of surgery was shorter in group A, 37 (8) minutes compared with 43 (7) minutes in Group F. No formal assessment of operating conditions was made but any comments made by the

Table 1. Age, weight and medications taken.

	Group A	Group F
Age, years, mean (SD) (range)	76 (8) (64–91)	75 (8) (53–91)
Weight, kg, mean (SD)	66 (11)	68 (13)
ASA 1/2/3	3/13/3	3/13/4
Males : females	2 : 17	5 : 15
Medication		
Diuretics	2	6
β-adrenoceptor blockers	4	0
Calcium channel blockers	2	2
α_2 adrenoblockers	1	1
Anti-arrythmics	1	2
Bronchodilators	3	1
Oral hypoglycaemics	2	2
Insulin	0	1
H_1 blockers	0	2
Tranquillisers	1	3

Table 2. Pre-operative values of intra-ocular pressure (IOP), systolic arterial pressure (SAP), $Paco_2$, oxygen saturation are mean (SD).

	Group A	Group F
IOP (mmHg)	16.7 (2.4)	15.8 (3.8)
SAP (mmHg)	157 (14)	155 (26)
$Paco_2$ (kPa)	5.25 (0.39)	4.99 (0.45)
O_2 saturation (%)	95 (2)	94 (4)

Table 3. Incremental doses of sedation.

	Number	Incremental dose (ml) mean (range)	Time (minutes) elapsed after initial sedation (mean)
Group A	5	1.6 (1–3)	22
Group F	5	1.6 (1–2)	25

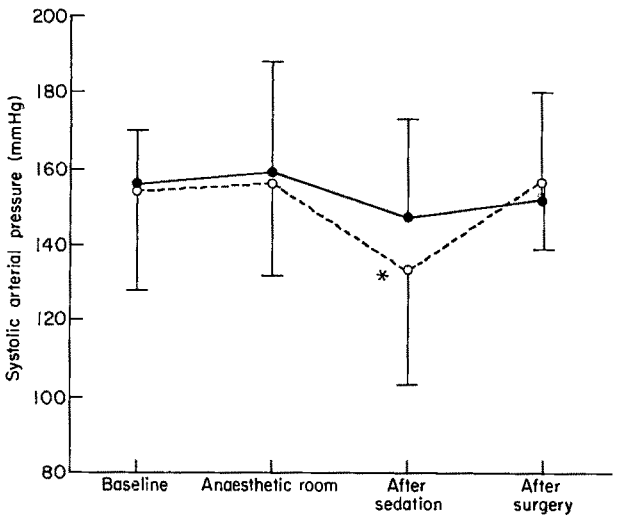

Fig. 2. Systolic arterial pressure (mmHg), mean, SD. Group A, (●—●); Group F (o---o). *$p < 0.05$ compared with anaesthetic room value (within-group difference).

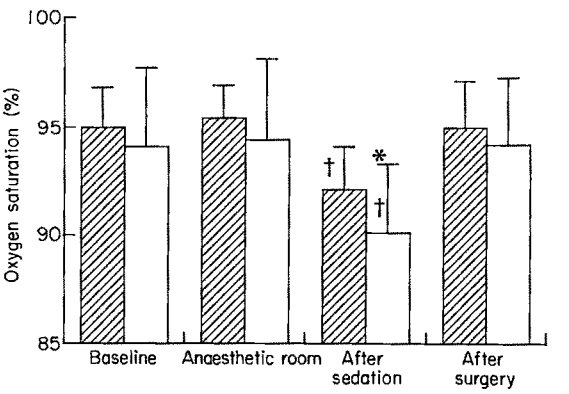

Fig. 3. Oxygen saturation (%) mean, SD. Group A, ▨; Group F, □. *$p < 0.05$ between-group differences; †$p < 0.0001$ within-group difference compared with baseline.

surgeon were noted. The ophthalmologist gained the impression of a high IOP intra-operatively in one case in group A. This was not confirmed either before or after operation by measurement, and $PaCO_2$ was not elevated. There was no nausea, vomiting or need for any post-operative analgesia in either group.

Discussion

The small decrease in IOP seen in both groups after premedication is not significant in clinical terms, since IOP can vary by up to 3 mmHg under normal conditions; there was no correlation between this decrease and the dose of premedication given. There is very little published work on this topic, but Trew *et al.*[8] concluded there was no significant change in IOP between patients given oral diazepam or ascorbic acid 90 minutes before operation, although intravenous diazepam may decrease IOP transiently.[9,10]

The results of the study demonstrate that there was a significant and similar decrease in IOP in both groups after intravenous sedation; this decrease was maintained until the end of the study period. Our findings contrast with those of Mostafa *et al.*[6] who noted a greater decrease in IOP with alfentanil during general anaesthesia.

Retrobulbar and facial nerve blocks were performed by an experienced surgeon and in no case was there concern about the adequacy of the block. Retrobulbar block with local anaesthetic should cause some relaxation of extra-ocular muscles and thus may lead to a decrease in IOP. Breslin *et al.*[11] found a decrease in IOP 4 minutes after such a block, but it was not significant. Thus any relaxation of extra-ocular muscles due to the local nerve block is unlikely to account for the significant decrease in IOP noted in this study after sedation. Retrobulbar block carries a significant risk of respiratory depression, probably due to intradural injection.[12] It is important, under these circumstances, to choose a sedative technique which does not compound the tendency to respiratory depression. The increase in $PaCO_2$ within each group was statistically significant, and although this was slightly greater in group F this was clinically unimportant in the patients studied. Four patients were taking bronchodilator therapy, although none had severe respiratory disease; the increase in $PaCO_2$ may be more relevant in those with more marked respiratory impairment. An increase in $PaCO_2$ leads to a rise in IOP and a close linear relationship exists between the two.[13] The increase in $PaCO_2$ observed in both groups after sedation was not sufficient to exert any significant effect on IOP. This is supported by the fact that IOP at cessation of surgery was the same as after the initial administration of sedation.

Oxygen saturation after intravenous sedation was lower in group F than in group A. Severe desaturation was not common, although this effect is important. Little published information exists on saturation during sedation for ophthalmic surgery under local anaesthesia. The apparently greater effect of fentanyl cannot be explained in terms of a comparatively greater dose. It is possible that this peak effect of fentanyl coincided with the postsedation measurement, when that of alfentanil had passed.[5] However, saturation increased on application of oxygen via the modified facemask and was similar in both groups at the end of surgery. This underlines the importance of oxygen administration to patients in this situation. Smith and Crul[14] have asserted that major regional block combined with sedation should be accompanied by oxygen administration and pulse oximetry. This advice may be extended to the situation under consideration.

Postsedation measurements were made when the patient was drowsy but easily rousable, as assessed by the anaesthetist (A.E.M.). This point was standardised as far as possible, in that the same anaesthetist (who was unaware of the group allocation) prescribed premedication and administered sedation and was unaware of group allocation in all cases, according to routine clinical practice. The time taken to reach this point was variable and thus IOP and systolic arterial pressure were measured at a variable time interval after the administration of sedation.

No decrease in arterial pressure was seen in group A. This may be explained by the more transient action of alfentanil compared with fentanyl;[5] any decrease in pressure and subsequent recovery occurred more quickly and was therefore missed by this protocol. However, there were no between-group differences. IOP does not correlate with systolic arterial pressure in this or other studies.[2,8]

IOP was measured by the same surgeon for each patient and by two surgeons throughout the study; there was no difference between the results obtained by the two separate surgeons. The Perkins hand-held tonometer was first described in 1965,[7] and determines ocular tension by defining the amount of pressure required to flatten the cornea, i.e. it is an applanation tonometer. It gives accurate readings and is portable.

Fentanyl and droperidol are routinely used in this unit. The addition of droperidol to the analgesic improves the

quality of sedation and is also an antiemetic; it is used commonly in ophthalmic anaesthesia in this respect, and we could not justify its exclusion. Feneck and Durkin[2] found no difference in IOP in patients given fentanyl with or without droperidol as part of a general anaesthetic technique.

The relative dosage chosen for alfentanil and fentanyl was that recommended previously.[15] This supports the relative dose ratio, since there was no significant difference in the volume titrated to a fixed end-point between each group. No patient required postoperative analgesia, a common finding after such surgery.

Sedation with alfentanil and droperidol causes a reduction in IOP similar to that produced with fentanyl and droperidol. It has less of an effect on $Paco_2$ and oxygen saturation when used in the dosage and manner employed in this study. Alfentanil and droperidol forms a suitable regimen for intravenous sedation in conjunction with local anaesthesia for intra-ocular surgery.

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Acupuncture anaesthesia

Observations on its use for removal of thyroid adenomata and influence on recovery and morbidity in a Chinese hospital

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Summary

Acupuncture anaesthesia, supplemented by small doses of pethidine, was evaluated in 20 patients who had surgery for removal of a thyroid adenoma. There were significant increases in mean arterial pressure and respiratory rate during surgery, but no significant change in heart rate. The mean dose of pethidine given during surgery was 45 mg (SD 8.9). Postoperative recovery was rapid and complication free. Acupuncture anaesthesia did not provide complete analgesia, but was safe and preferable to general anaesthesia where there was a shortage of facilities.

Key words

Anaesthetic techniques; acupuncture.

Acupuncture anaesthesia was introduced in 1958 and became a commonly used technique in China. The technique elevates the pain threshold sufficiently to allow surgery on conscious subjects[1] and many articles are published which describe its use during thoracotomy,[2,3] abdominal surgery[4,5] and even paediatric surgery.[6] Experi-

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ence with more than 2 000 000 cases was reported at a symposium in Beijing in 1984. Many Western scientists were invited to China to witness the technique, but their reports were limited to only a few cases,[7] or based on a fleeting contact with the method.[8–19]

Until the late 1970s up to 80% of surgical procedures in China were performed under regional anaesthesia; acupuncture was used in 8–30% of these cases.[8,20] Nowadays the technique is only used routinely for procedures such as operations on the head and neck, in neurosurgery and for removal of thyroid adenomas. Acupuncture anaesthesia alone can be used in 95.4% of the latter procedure[21–23] and it was possible in recent years to evaluate the method more closely and to follow patients pre-, per- and postoperatively. This has led to the present study on the evaluation of acupuncture anaesthesia for removal of thyroid adenoma. The study protocol was designed after consultation between the Departments of Anaesthesia of the University of Nijmegen and the First Affiliated Hospital of Nanjing Medical College, China. The study protocol was approved by the ethics committee of the latter hospital, which was visited from April to June 1987.

Methods

Twenty consecutive ASA 1 or 2 patients scheduled for removal of thyroid adenoma were studied. Informed verbal consent was obtained at the pre-operative visit. Psychological preparation and pain-threshold tests[23] were not carried out. Routine investigations for this type of surgery were obtained.

Patients were premedicated with diazepam 10 mg orally 90 minutes before surgery, after fasting overnight. An intravenous infusion was set up and 10 minutes later a blood sample was taken from the other arm to exclude the presence of pethidine. The sample was frozen and the analysis carried out in Nijmegen using an HPLC method which had a detection limit of 10 ng/ml.[24]

Acupuncture was performed by the same anaesthetist (C.F.Z.) in each case. Four ear points on the same side as the thyroid adenoma were selected for puncture (Table 1, Fig. 1). The needles were connected to a battery-powered G-6805 acu-stimulator whose output could be varied arbitrarily from 0–4. Stimuli at a rate of 4 Hz were applied and the strength gradually increased to the limits of the patients' tolerance. The maximum amplitude reached was setting 3 in all cases, which resulted in a current up to 20 mA and voltage up to 20 volts.

Pethidine 30 mg was given intravenously 15 minutes after the start of stimulation. Surgery started 30 minutes after the start of stimulation and continued until the end of the procedure. Further small doses of pethidine together with a small dose of chlorpromazine were given intravenously if the arterial blood pressure and/or heart rate increased by more than 25% during surgery; in some cases procaine was infiltrated into the wound. The dose of pethidine did not exceed 1 mg/kg. Arterial blood pressure, heart rate and respiratory rate were recorded before acupuncture anaesthesia, after 15 minutes of stimulation, at the time of skin incision and at 10-minute intervals thereafter. These variables were also recorded every 15 minutes during the immediate recovery period. The ECG was continuously displayed, while pain was measured on a verbal scale of 0–3 (0, no pain, 3 severe pain) at regular intervals.

Pethidine was available for analgesia after operation and there was no restriction on mobility or oral fluid intake. The patient, surgeon and anaesthetist were asked to assess the quality of analgesia as good, satisfactory or unsatisfactory immediately after surgery. The patients were asked again to evaluate the anaesthetic on the first, second and third postoperative days. In addition, their daily activities such as getting out of bed, ability to go to the toilet were recorded and they were also asked to assess their fatigue level on a linear visual-analogue scale with extremities labelled 1, fit and 10, exhausted. The incidence of any complications was also noted.

Data were analysed using the General Linear Models for repeated measures and Pearson's correlation test; $p < 0.05$ was regarded as significant.

Results

Details of the patients and duration of surgery and anaesthesia are shown in Table 2. All pre-operative investigations were within normal limits. Pethidine was not found in any of the pre-operative blood samples.

The changes in mean arterial pressure, heart rate and respiratory rates are shown in Figure 2. Mean pressure was significantly higher than control after 15 minutes of stimulation (point C, Fig. 2) and remained elevated by up to 20% during the entire course of surgery ($p < 0.01$). Mean arterial pressure was also significantly higher than pre-operative values in the immediate recovery period. In contrast, heart rate remained stable throughout the study period with no significant changes from control. One hypertensive patient developed a bradycardia of 30 beats/minute immediately after skin incision and was given atropine.

Respiratory rate was significantly increased throughout surgery, but not in the immediate postoperative period. The increase in respiratory rate correlated with an increased pain score ($p < 0.05$). No patient complained of pain at the time of surgical incision. The highest pain score (1.2, SD 0.8) was noted 10 minutes after incision, and the scores remained elevated throughout surgery. Sixty minutes after surgery, the mean pain score was 0.1 (SD 0.2).

The supplementary drugs given are shown in Table 3. Only five patients required no further medication. The mean dose of pethidine given to the remaining 15 patients was 45 mg (SD 8.9). Chlorpromazine was given to reduce arterial blood pressure in four patients. Infiltration with procaine was used in three patients; this was needed in two because surgery was extended to perform a lobectomy.

The assessment of analgesia is shown in Table 4. Analgesia was judged unsatisfactory by the anaesthetist on only

Table 1. Localisation of ear points used at the First Affiliated Hospital of Nanjing Medical College, China, for the surgical removal of ipsilateral thyroid adenoma.

Name of point	Auricle area	Anatomical location
Jiaogan (sympathetic nerve)	Inferior antihelix crus	At junction of inferior antihelix crus and medial border of helix
Jing (neck)	Antihelix	At junction of antihelix and antitragus, near scapa
Neifenbi (adrenal)	Tragus	At lower tubercle on border of tragus
Shenmen	Triangular fossa	At bifurcation point of superior antihelix crus and inferior antihelix crus

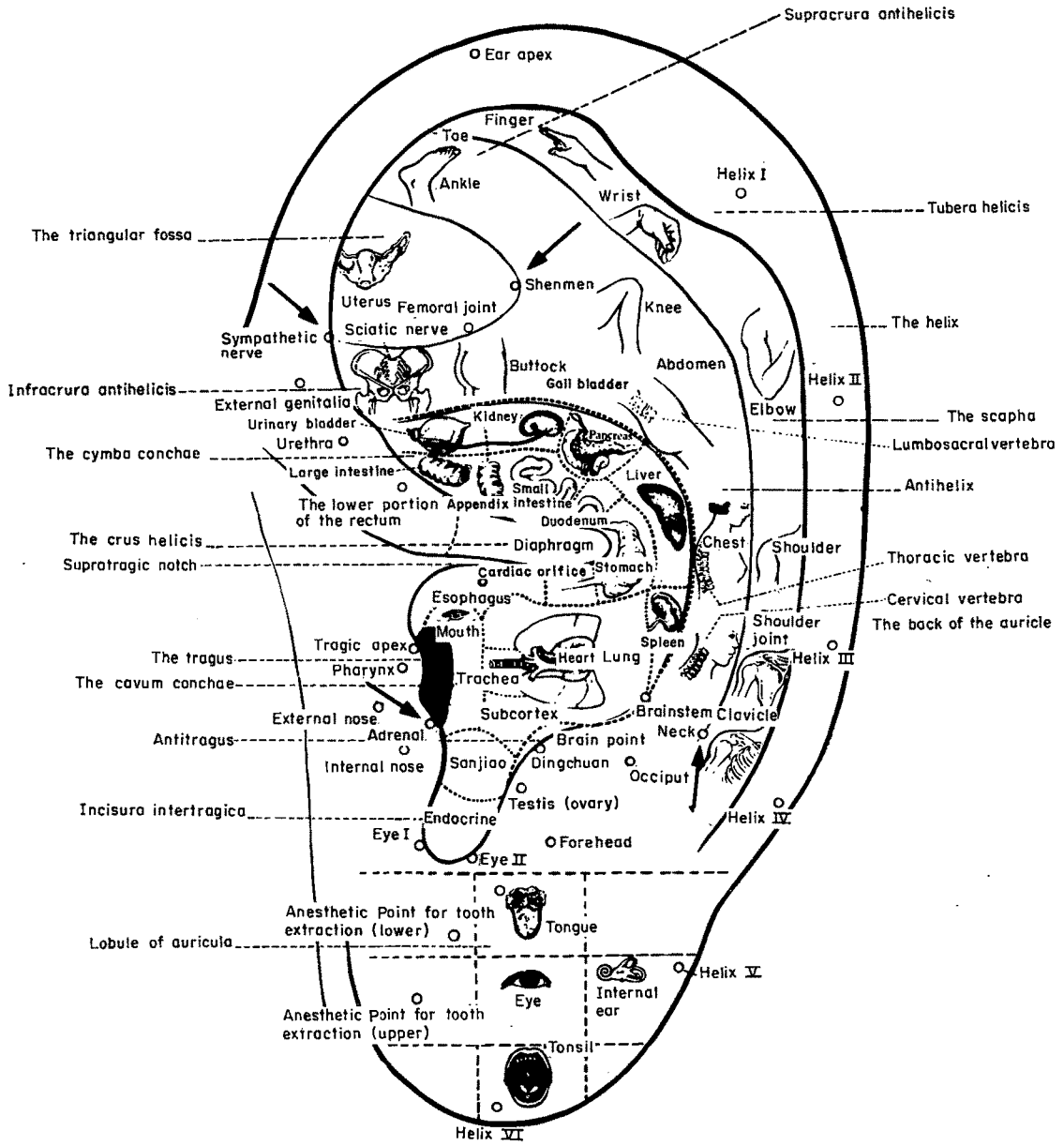

Fig. 1. Ear points used for surgery. Arrows indicate the points chosen for removal of ipsilateral thyroid adenoma.

one occasion when a thyroid lobectomy had to be performed.

Surgery was completed in all patients without recourse to general anaesthesia. There were no complications relating to surgery, although one patient coughed repeatedly during mobilisation of the gland. Twelve patients were noted to be sweating during surgery, while one patient was nauseated. One patient vomited in the recovery room. The overall assessment of the anaesthetic technique by the patients is shown in Table 5.

The postoperative pain scores are shown in Figure 3. The majority of patients were pain free and none experienced severe pain. Pethidine was not used in any patient. Only one patient did not get out of bed on the first postoperative day. The fatigue score was 3.2 (SD 1.4) on the first day after surgery and had decreased to 1.4 (SD 0.6) by day six.

Table 2. Details of patients included in the study, surgical and anaesthetic time and pre-operative values of haemoglobin and haematocrit. Data represent mean values and (SD).

Age (years)	38.8 (11.5)
Weight (kg)	58.8 (9.5)
Height (cm)	161.3 (5.7)
Sex M/F	2/18
ASA status 1/2	16/4
Adenoma to be removed	
size (cm × cm)	1.2 (0.4) × 2.3 (0.9)
localisation: L/R	9/11
Surgical time (minutes)	88.8 (44.3)
Anaesthetic time (minutes)	127.7 (46.1)

Discussion

The increases in arterial pressure found during acupuncture anaesthesia and surgery in our patients were limited to 20%; this confirms the work of others.[21,25] We noted that more pronounced increases occurred in two hypertensive patients, which is similar to that which occurs during balanced general anaesthetic techniques[26] and indicates that pre-operative treatment of hypertension is also necessary before acupuncture anaesthesia.

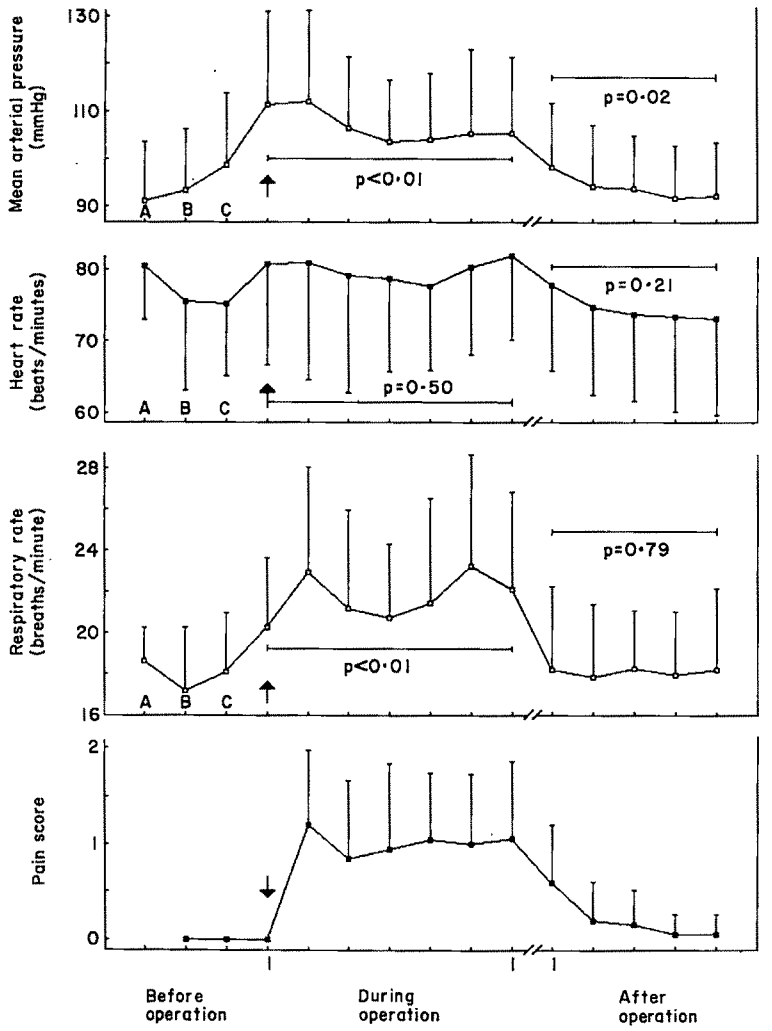

Fig. 2. Changes in mean arterial pressure, heart and respiratory rates and pain scores. Figures are mean (SD). A, at hospital admission; B, before acupuncture stimulation; C, 15 minutes after stimulation; arrow, start of surgery.

No significant changes occurred in heart rate during surgery, although one patient developed a marked bradycardia. It has been suggested that heart rate is a reliable indicator of pain in conscious subjects during acupuncture anaesthesia.[27] There are so many factors that influence heart rate that changes cannot be reliably related to the amount of pain experienced. A stable heart rate does not imply the absence of pain as shown in this study. There was, however, a significant correlation between respiratory rate and pain scores.

No patient complained of pain at the time of incision, a feature that has been noted by others.[8,28] Acupuncture during surgery was unable to provide total analgesia, but all patients remained quiet and calm on the operating table and surgery was completed in all cases. Such a state of affairs would not occur in Western countries, although in selected patients acupuncture anaesthesia has been used

Table 3. Supplementary drugs used during surgery.

Drug	Number	Dose
Pethidine	14	20 mg
	1	10 mg
Chlorpromazine	1	3 mg
	3	2 mg
Atropine	1	0.5 mg
Local anaesthetic (procaine 0.5%)	1	5 ml
	1	10 ml

Table 4. Assessment of analgesia by surgeon, patients and anaesthetist in the immediate postoperative period.

Quality of analgesia	Surgeon	Patient	Anaesthetist
Good	18	7	8
Satisfactory	2	13	11
Unsatisfactory	0	0	1

Table 5. Overall assessment of the anaesthetic technique used as judged by patient when questioned on days 1, 2 and 3 after operation.

Anaesthetic technique	Number of response		
	Day 1	Day 2	Day 3
Good	6	10	12
Satisfactory	12	8	8
Sufficient	2	2	0
Bad	0	0	0

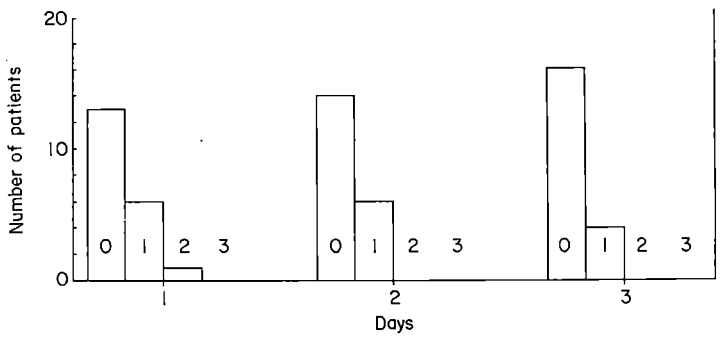

Fig. 3. Incidence of no (0), mild (1), moderate (2) and severe (3) pain on the first 3 days after operation.

successfully for a number of different operations.[29–34] Additional drugs were required in the present series, but the amounts used were very small compared to other studies when thyroid surgery was performed under local anaesthesia.[35,36]

One of the commonest problems of thyroid surgery under local anaesthesia is laryngeal spasm associated with traction on the trachea.[35,36] This was not seen in any of our patients, although one did cough during the procedure. The overall incidence of minor complications was also low and the technique was generally acceptable to patient, anaesthetist and surgeon.

The present study has shown that it is possible to perform thyroid surgery under acupuncture anaesthesia in Chinese patients. However, it is important that patients are aware of, and accept, the fact that analgesia may not be complete throughout the entire procedure. Also the anaesthetist must be prepared to give analgesics intravenously and the importance of gentle surgery is stressed upon the surgeon.

Acknowledgments

This study was supported by the Division of Scientific Exchange with China of the Dutch Ministry of Education, Janssen Pharmaceutica and the Research Foundation of the Institute of Anaesthesiology of the University of Nijmegen. We also thank the Chinese Authorities for the opportunity to perform this study in Nanjing, China, Hewlett Packard for supplying the ECG monitor and Drs P. Allen, P.W.C. Kloppenborg and L.H.D.J. Booij for critical review of the manuscript.

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Problems with the Mallampati sign

Mallampati[1] described a simple, quick method to predict difficult tracheal intubation. The test has achieved considerable popularity but the serious limitations need to be appreciated.

The test depends upon which pharyngeal structures are visible when the patient's mouth is opened and the tongue protruded. If the base of the tongue obscures the view then it may also obscure the view of the larynx and cause intubation to be difficult.

Problems associated with the test include observer variability, unsatisfactory results and omission of the cervical mobility.

We asked nine anaesthetists to assess the same 10 colleagues using Samsoon and Young's diagram[2] and method. The extent of the agreement between anaesthetists for each subject is presented in the table. This shows the number of anaesthetists who agreed upon a particular pharyngeal class for each subject. Subject B for example is assessed as Class I by eight anaesthetists and class II by one anaesthetist (perfect agreement is represented by a 9, subject A). Note that as many as four of the subjects were classified as potentially difficult to intubate by at least one anaesthetist, and for two of these subjects (H, I) several anaesthetists disagreed.

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Table 1. The number of anaesthetists who agree upon a particular pharyngeal class for each subject using Samsoon and Young's modification[2] of the Mallampati sign (see text).

	Visibility of pharyngeal structures										
Class											
IV	0	0	0	0	0	0	0	1	0	1	Difficult
III	0	0	0	0	0	0	1	2	3	0	
II	0	1	3	3	4	6	6	2	4	5	Not
I	9	8	6	6	5	3	2	4	2	3	Difficult
Subject	A	B	C	D	E	F	G	H	I	J	

One source of variation is ambiguous definition of the classes. It is not clear from Mallampati's description[1] if inability to see the faucial pillars or masking of the uvula indicates class III. Samsoon and Young require loss of fauces but allow the base of the uvula to be seen for this class. Samsoon and Young[2] created an additional class IV in which the soft palate is completely obscured, although the anterior border of the soft palate has no readily discernible landmark (in fact, they used an imaginary line joining the anterior edge of the fauces; personal communication). Their figure provides a helpful visual classification.

Another very important source of variation is the response of the patient to the instructions. Many automatically say 'Ah' or simulate phonation, which falsely improves the view. Others arch the tongue which obscures the uvula. Two attempts are recommended to overcome these problems, but it is not easy to know if the assessment is made at a time when the patient's response is appropriate.

Mallampati[1] suggests that difficult intubation is associated with grade III view of the larynx (failure to see beyond the epiglottis) and this is predicted by a class III view of the pharynx. In his original study only 55% of difficult laryngoscopies were correctly identified and in a more recent, larger study[3] ($n = 666$) the proportion was only 44%. Over half of the difficult patients were missed!

Charters, Perera and Horton[4] abandoned the test after their prediction that 22% (13/60) of their patients would be difficult when only one proved to be difficult. In our own experience 53% (66/122) were falsely predicted as difficult and all three patients in whom laryngoscopy was difficult were missed. A method for prediction of difficult intubation, previously described by one of us,[5] was also used for comparison: all three difficult patients were identified with 17% false alarms.

Head and neck mobility is not assessed by the test. However, limited movement, especially of the atlanto-occipital joint, is a common cause of difficult intubation.[6]

We maintain that the vital distinction between class II and III depends upon a wavering, ill-defined boundary that causes considerable observer variability. The identification of a class III patient may warn of an impending problem, although many false alarms will occur. A class IV obstetric patient, especially if associated with limited head and neck movement, will almost certainly be difficult to intubate and a junior should summon assistance (Samsoon and Young, unpublished prospective study).

Difficulty with intubation is caused by many factors. It is a worry that many difficult patients will be missed, especially if head and neck mobility is not assessed.

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Kinking of the laryngeal mask airway in two children

The Laryngeal Mask Airway (LMA)[1] is used in a variety of situations in anaesthesia. We wish to draw attention to a potential hazard of its use.

A 3-year-old boy was anaesthetised for computerised tomography (CT) of the head and neck. Anaesthesia was induced with nitrous oxide, oxygen and isoflurane, and a size 2 LMA inserted. The cuff was inflated with 5 ml Neopam nonionic contrast medium as part of another study, and the patient positioned supine with the head slightly flexed. The airway was clinically clear and the oxygen saturation 98%, measured by pulse oximetry.

The lateral CT image showed the LMA to be correctly located over the larynx; however, the tube was noted to be kinked and partially obstructed at a point approximately 1.5 cm above the cuff (Fig. 1). The patient was examined but there was no clinical evidence of obstruction. There was no evidence of turbulent flow on listening at the end of the airway, and the oxygen saturation remained at 98%.

A second patient was anaesthetised by the same technique on a subsequent occasion using the same sized LMA. Similar kinking was seen on the CT scan and, as with the first case, there was no clinical evidence of obstruction.

It was possible in each case, after removal of the LMA, to demonstrate identical kinking by flexing the device to the angle seen on the scan. This was repeatable with either contrast medium or air in the cuff. Kinking was demonstrated in both our size 2 LMAs; however, we were unable to kink our size 1, 3 or 4 laryngeal masks, even with extreme flexion. The masks were new, and had not been autoclaved before use. The manufacturers are aware of the problem.

This is the first described use of CT to show positioning of the LMA in paediatric patients. Kinking of a size 2 LMA was demonstrated in two patients having scans with the device in place. Clinical observation failed to reveal an incipient obstruction, therefore, it is important to avoid

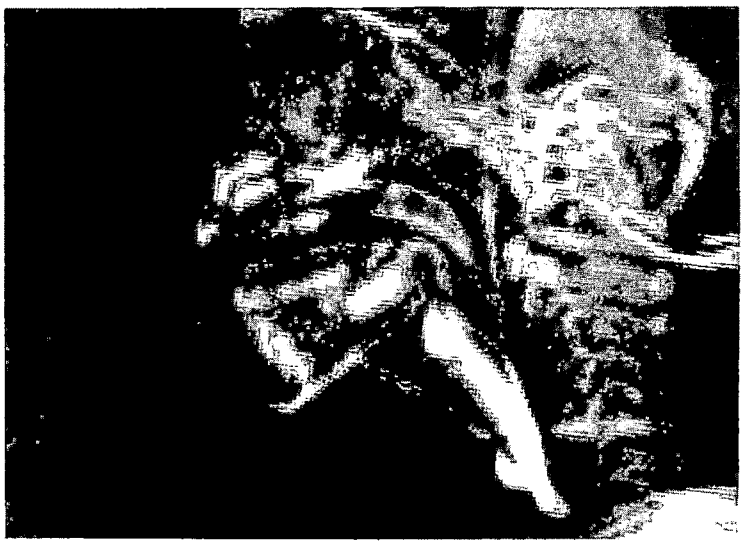

Fig. 1.

complacency in using this valuable new aid to airway management.

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A reply

We are grateful to Drs Goldberg, Evans and Filshie for drawing our attention to the tendency of the size 2 laryngeal mask to kink. The silicone tubing in all the sizes is internally ridged, which may reduce the degree of obstruction if kinking occurs. This may explain the normal oxygen saturation and clinically clear airway in the two patients described. However, the manufacturing process is now being altered to increase the kink resistance of the size 2 mask. Meanwhile, all users should exercise extra caution and avoid neck flexion when using the existing size 2. Further sales of size 2 will resume when the product has been appropriately modified.

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Recurrent bradycardia due to latent sick sinus syndrome

A 57-kg, 83-year-old woman was scheduled for excision of an infra-orbital basal cell carcinoma. She complained only of breathlessness on exertion. She took nitrazepam at night. Cardiorespiratory examination and investigations including 12-lead ECG were normal. No premedication was prescribed.

The heart rate before induction was 80 breaths/minute and she was in sinus rhythm. Glycopyrronium 0.2 mg preceded alfentanil 0.75 mg, vecuronium 4 mg, and propofol 100 mg. Tracheal intubation was achieved after 2 minutes' ventilation of her lungs with enflurane 1% in oxygen.

ECG in theatre showed sinus bradycardia at first: the rate was 35 breaths/minute. Long sinus pauses and a slower nodal escape rhythm developed. Spo_2 was 98%, although systolic pressure was 40 mmHg by automated oscillotonometry. A total of 1.2 mg atropine intravenously had no effect. Methoxamine 5 mg, immediately available, increased the blood pressure to 120 mmHg without an alteration to heart rate. Eight microgrammes of isoprenaline, however, restored the rate to 80 breaths/minute. The inspired oxygen was reduced to 50%, ventilation of the lungs with N_2O and enflurane 1.5% maintained $P_E'CO_2$ at 4.0 kPa. The operation then commenced and heart rate was stable for 20 minutes until, unrelated to surgical stimulation, it slowed again. On this occasion, and at approximately 15-minute intervals, it was corrected by isoprenaline 6 μg. Additional vecuronium was withheld despite full recovery of neuromuscular function at an early stage. No anticholinesterase was given. The patient's recovery was uneventful.

The initial bradycardia was thought to be drug-induced. Its recurrence in the absence of any increments suggested pre-existing cardiac pathology. Twenty-four hour ambulatory ECG monitoring revealed long periods of profound bradycardia, which included sinus pauses and nodal escape rhythm. This established a diagnosis of sick sinus syndrome.[1] A relative asserted that the patient suffered from dizziness which occasionally caused loss of balance. Therefore, a permanent pacemaker was implanted.[2]

Bradycardias associated with vecuronium,[3] alfentanil,[4] and propofol[5] are described. Pretreatment with an anticholinergic agent might be expected to reduce the incidence of bradycardia in normal individuals. However, impaired responses to atropine are known to occur in patients with sinus node disease.[6] Bradycardia in this case was neither prevented by 0.2 mg glycopyrronium, nor responsive to 1.2 mg atropine, but was successfully treated with small doses of a β agonist.

It should not be assumed that bradycardia under anaesthesia is necessarily iatrogenic. The cause might be sick sinus syndrome.

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A re-evaluation of the Whitacre spinal needle in obstetric anaesthesia—a pilot study

The use of spinal (subarachnoid) anaesthesia in obstetric patients is limited by the high incidence of postspinal headache in young pregnant patients.

The aetiology of the headaches is still obscure. They are thought to be associated with a leak of cerebrospinal fluid through the dural puncture site and therefore related to the size of the hole made. The reduced production of cerebrospinal fluid in the period of puerperal diuresis may be the reason for this very high incidence of headaches in obstetric patients.

H.M. Greene[1] proposed in the early 1920s that a change of the point of the spinal needle to a rounded shape would cause less damage to the dural fibres. Hart and Whitacre[2] suggested that a similar needle 'which would separate or penetrate in a way a cambric needle penetrates fabric, would be less traumatising than a needle which cuts or tears the fibres of the dura'. On withdrawal of the needle the fibres should 'quickly return to a state of close apposition' and thereby reduce leakage. The result of their work was the introduction of the Whitacre pencil point needle. This is a 20-gauge needle with a solid end drawn to a point similar in shape to a finely sharpened pencil and with an opening proximal to the tip. Use of this needle halved the incidence of postspinal headache.

Recent *in vitro* work by Cruickshank *et al.*[3] and Ready *et al.*[4] has now confirmed Greene's suggestions and shown a difference in cerebrospinal fluid loss when comparing cutting (Quincke) and rounded (pencil point) needles. The latter, as suspected, caused the smaller loss.

We have recently used spinal anaesthesia more frequently because of the high success rate and better quality of anaesthesia compared with that after epidural anaesthesia. Postspinal headache[5] has remained a problem. We have therefore used smaller gauge needles. These are known to produce a smaller incidence of spinal headache, but their insertion requires greater skill and technical failures are more common. We thought it might be useful to assess the Whitacre pencil point needle now produced in a 22-gauge form. We wished to determine if its use enabled the anaesthetist to detect dural puncture easily, provided a rapid reflux of cerebrospinal fluid to confirm accurate placement and was associated with a low incidence of postspinal headache.

Nineteen needles were used for a variety of obstetric procedures (Table 1). The needles were used by a number of registrars of varying experience under everyday working conditions. Each anaesthetist was asked to comment on the use of the needle and to record the number of attempts necessary for successful placement as well as any problems encountered.

All patients were allowed to mobilise after the return of full motor function. Each patient was visited or telephoned at home by an anaesthetist daily for at least 5 days after spinal anaesthesia and actively questioned about any headache.

Table 1.

Procedure	Number of needles used	Greatest number of attempts to place	Number of headaches	Number of postural headaches
Caesarean section	17	1	0	0
Suture of perineum	1	1	1	0
Forceps delivery	1	1	0	0

All needles were successfully placed on the first attempt. Everyone, however, commented that introduction and placement felt very different from that when the Quincke needle was used. None of the 19 patients developed a postural headache.[3]

It seems to us that the perfect spinal needle for obstetric anaesthesia should provide simple and accurate insertion with the production of a rapid and profound block with minimal side effects. We believe that the Whitacre pencil point needle may have these advantages. This needle may therefore have a useful place in obstetric anaesthesia and further investigation will determine its exact role. The numbers in our study are too small to make any comparative assessment, but we are encouraged by our favourable results with the 22-gauge needle so far, and a larger controlled study is now being undertaken.

The needles used were the 'Whitacre Needle' and we express our thanks to Vygon UK Ltd. for obtaining and supplying us with these needles.

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Occupational exposure to nitrous oxide in four hospitals—a comment

The paper with the above title by Gray (*Anaesthesia* 1989; **44:** 511–4) gives a gloomy view of the efficiency of the equipment usually employed to reduce atmospheric pollution by waste anaesthetic gases or vapours. The staff who administer anaesthetics in four hospitals in Glasgow were found to be exposed to nitrous oxide in concentrations which would be unacceptable in those countries in which there are specific regulations that relate to environmental control. The author assumes that the state of affairs in these hospitals was no worse than that in any other part of the western world where similar methods are used to avoid this hazard, whether or not it is in fact harmful. One reason for this may be that anaesthetic and dental staff may look upon the scavenging systems employed as cumbersome and intrusive upon their treatment of the patient.

One wonders why inadequacy of the air conditioning system is held responsible, as well as of the scavenging system, when it was demonstrated in 1980[1] that even 20 changes of air per hour was of minor importance in the reduction of atmospheric pollution to an acceptable level. An efficient collection system attached to the expiratory (APL) valve is also of no avail when the nasal inhaler (facepiece) fits the face badly. This is a common feature of dental chairside anaesthesia, especially during the end expiratory phase when positive pressure in the breathing system has to overcome the resistance of the expiratory valve. Any manipulation around the patient's air passages by the dentist or anaesthetist may necessitate temporary removal of the inhaler, and cause a cloudburst of nearly undiluted anaesthetic gases to follow the line of least resistance, and, instead of passing through the expiratory valve, to fall upon the anaesthetist's face.

A suction (aspiration) system is now being introduced to overcome this unsatisfactory situation. This consists of a funnel installed 20 cm above the patient's face with a constant displacement of 2500 litres/minute. This funnel may be suspended from either the wall or the ceiling: it does dictate the precise location where the anaesthetic is given and is intended to be used in addition to the collection system on the expiratory valve and not to replace it. This local suction can be bought for half the price of an anaesthetic trolley; no information is given about the level of noise it produces.

A double facepiece is manufactured to prevent leakage around the patient's face. There is a space between the facepiece and the patient end of the breathing system from which waste gases are carried to the exterior via a widebore corrugated hose. It is powered by a fan (individual to each place of work) to give a displacement of about 500 litres/minute. Again, no information is given about the level of noise that it produces.

Many inventions have seen the light of day which are inconvenient and costly to the anaesthetist and of benefit only to the manufacturer.[2]

The attempt to produce scavenging systems based on the concept of collection of waste gases after they have been voided to the room air has proven to be impossible. The solution is to remove the gases from the point at which they are used and to discharge them where they can do no harm. This can be achieved only by removing the gases from the breathing system at the same rate as the fresh gas inflow. This may be done with the ejector flowmeter.[3,4] This instrument may be connected to the breathing attachment by narrow-bore tubing. It is appropriate for all types of breathing systems, including those for paediatric, dental and obstetric use.[5] It is powered by compressed air at 300 kPa, and affords continuous surveillance and control of gas evacuation from the breathing attachment, with flow rates of up to 15 litres/minute. This fulfils all clinical requirements. It permits active emptying of the breathing attachment before it has to be disconnected from the patient in contrast to all other scavenging devices. Therefore no extra scavenging is required. The gas flow rate in this device is low and produces no noise. It complies with all national requirements that relate to the anaesthetic environment.

All manufacturers in the western world were presented with information about this method several years ago, but so far only those in Denmark have shown any interest.

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A reply

My survey did indeed show that many of the staff monitored received nitrous oxide exposures that would be unacceptable in Scandinavian countries, in which there is a statutory limit of 100 ppm for an 8-hour time-weighted average exposure. Dr Jørgensen shows understandable enthusiasm in his advocacy that matters would be improved by the use of the ejector flowmeter, which he has developed. However, his letter contains some errors, one of which is crucial.

Dr Jørgensen twice misrepresents me. First, I did not 'assume that the state of affairs in these hospitals was no worse than in any other part of the western world where similar methods are used to avoid this hazard'. The pattern seen in Glasgow might, I suggested, be typical of the situation throughout Britain. Second, I did not state that inadequate theatre ventilation was jointly responsible for the high exposures but I did suggest that this may have been a contributory factor. This seems such an obvious possibility that it scarcely requires justification. Davenport *et al.*[1] found no correlation between pollution levels and nominal rates of room ventilation, but they did point out that this may have been because the ventilation was not performing to specification; such departures from nominal performance have been reported.[2] Other studies[3–5] have demonstrated that theatre ventilation systems can contribute to the reduction of pollution levels.

Dr Jørgensen's crucial error is his statement that the ejector flowmeter 'complies with all national requirements relating to the anaesthetic environment'. This is certainly not the case in the United Kingdom, where the 1987 British Standard[6] lays down performance and safety requirements that the ejector flowmeter does not fulfil. Regardless of whether or not these requirements are thought to be reasonable, it is understandable that British manufacturers are unwilling to produce a system that does not comply with the standard.

There is no doubt that operating theatre pollution is often unacceptably high. There are probably many contributory factors, of which the design of scavenging systems is one. Perhaps Dr Jørgensen's letter will stimulate some much needed debate on the matter.

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A test for the Manley ventilator

This is an idea that I have come to incorporate into my clinical practice. The Blease Manley ventilator is driven by the pressure generated in the backbar of the anaesthetic machine by the fresh gas flow. This pressure will typically exceed 10 kPa with the MP2.[1] A fault with the ventilatory system (including a Manley ventilator) which allowed hand ventilation but not mechanical ventilation has happened on two occasions to me. The fault eventually proved to be a leak within the backbar at high pressure, and the ventilator was perfectly normal.

The standard suggestions for pressure testing of the anaesthetic machine concentrate on detection of the action of high pressure blow-off valves.[2] This can be almost impossible in a noisy operating theatre. If the ventilator on the anaesthetic machine is of the Manley type, a low flow of fresh gas (1–2 litres/minute) should suffice to cycle the ventilator, but if a leak develops at high backbar pressures then the ventilator will not cycle. If high flows are used in testing the system, then a sufficient pressure may be developed in the backbar to activate the ventilator even in the presence of a small high pressure leak, although the volume delivered to the patient will necessarily be reduced.

This is a useful confirmatory check of the equipment, and adds very little to the time required for any other checks of the ventilator function.

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Single breath induction of anaesthesia

The inhalational induction technique using a single vital capacity breath with 4% halothane in nitrous oxide and oxygen requires a reservoir bag of 4-litre size.[1] This particular size bag is not, if at all, readily available in hospitals. The group of patients that can benefit most from this induction technique are young adults who have extreme needle phobia who undergo elective surgery. To overcome this problem of availability of the 4-litre size bag, two identical 2-litre reservoir bags from Mapleson A breathing system are used. They are joined together in series in the Mapleson A system (Fig. 1). This simple modification has worked equally well and safely on at least five occasions so far. It is also useful for pre-oxygenation with large (vital capacity) breaths.

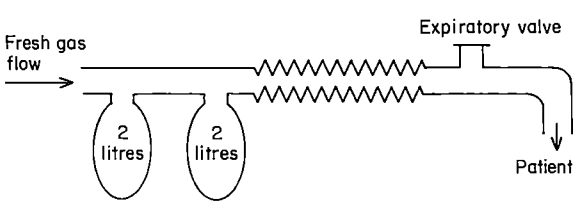

Fig. 1.

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Awareness and pain during surgery

The writer was the anaesthetist involved in the case discussed in a recent special article (*Anaesthesia* 1989; **44:** 352) and a few comments need to be added.

This case, which occurred in February 1986, came to public attention via a newspaper article,[1] in which the patient vividly describes her ordeal during surgery. It is well worth reading.

This incident occurred because I failed to realise what

was happening to my patient when the anaesthetic supply appeared to be correct. The oxygen flush control was not released after its use at the end of the previous case and I did not see this. There is no obvious indication that the oxygen flush control is operating on a Cape Waine Mk3, and it may not release if it is partially rotated when it is depressed.

A settlement of £20 000, with costs, was made within 3 months, and I, not the hospital, accepted full liability for the incident.

A 'Safety Information Bulletin'[2] was issued by the Department of Health in Northern Ireland. The assistance of the Safety Committee of the Association of Anasthetists of Great Britain and Ireland was required before a similar Bulletin could be issued in the remainder of the UK.

This potential hazard was first described in mid-1979[3] and most recently in late 1988.[4] When this incident occurred, the manufacturer had available an off-the-shelf modification kit. The hazard was known, the modification was available, however no contact was made with the end-user. A 'yellow card' system might speed up the process of hazard reporting and correction.

I met and talked with the patient and her husband for some time after the settlement. I explained how I had failed in my responsibility towards her to keep her asleep and pain-free, and the particular circumstances involved. She wrote to me shortly afterwards, and near the end of the letter writes: 'I can only say now that seeing you was a help to me and I hope that in some way it helped you.' It certainly did. She is a very brave woman.

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Design and evaluation of a new respiratory monitor

A variety of techniques for monitoring spontaneous ventilation exist. These are often awkward, technically complex, subject to motion, artifacts, or are expensive. Problems are especially severe when monitoring infants and children. We have designed a new breathing monitor which overcomes many of the objections to the previous designs.

The sensor consists of a small, thin-walled compressible silastic cylindrical chamber (Fig. 1) which is placed in the respiratory tract, typically in one of the nasal vestibules (Fig. 2). The open end of the chamber is connected via a long, small-bore plastic tube to a monitor that contains a sensitive pressure transducer. The warm expired air heats the sensor during expiration and increases the internal pressure, while during inspiration the ambient inspired air cools the sensor and reduces its internal pressure. These pressure variations are sensed by the transducer, converted to an electrical signal, processed electronically, and displayed on a bar-graph (Fig. 3). The beginning of each expiration is also indicated by an audible tone of adjustable intensity. An output jack on the monitor allows the respiratory signal to be displayed on an oscilloscope or recorded on tape or strip-chart recorder (Fig. 4). The unit is pocket-sized and is rechargeable.

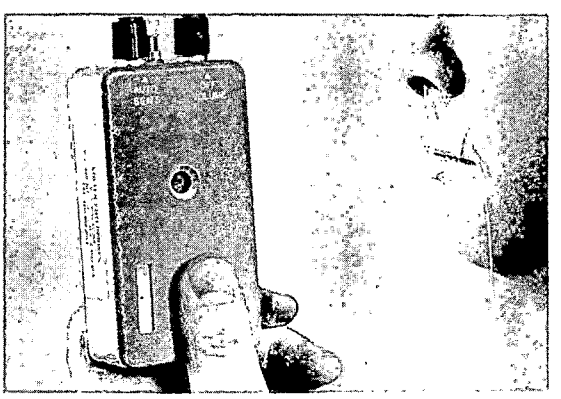

Fig. 2. Illustration of sensor in place. The monitor is held in the subject's left hand.

The monitor was used on 25 infants and children in a preliminary evaluation during transport from the operating room (OR) to the postanaesthetic recovery room (PAR). Immediately after extubation in the OR the sensor was placed adjacent to, or just inside, a nostril and taped to the cheek. The visual display and audio signal were available to

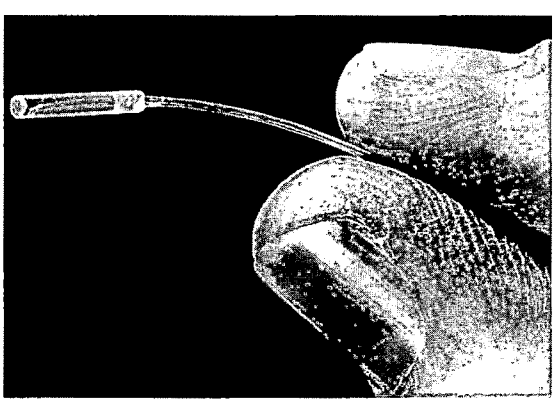

Fig. 1. Closeup view of the silastic breath sensor.

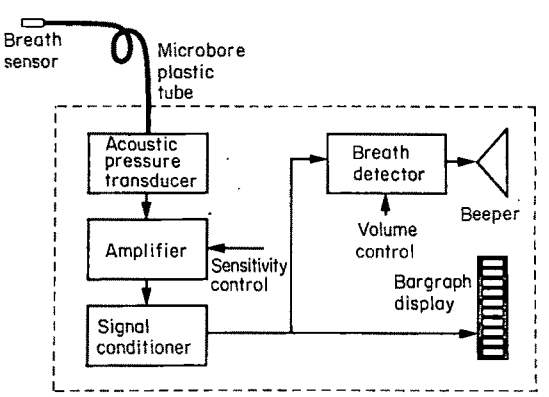

Fig. 3. Block diagram of the monitor.

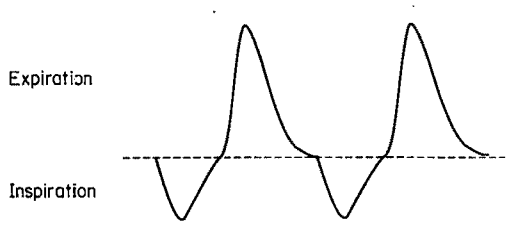

Fig. 4. Sample recording from the system.

the anaesthetist in addition to customary monitoring. A questionnaire was completed by the staff when the patient arrived in the PAR.

The patients studied were aged between 4 months and 15 years. The monitor was well-accepted by the medical and nursing staff and was found to be useful and reliable in 23 out of 25 cases. The small size, portability and simplicity of the monitor were the features most frequently favoured by the users.

The monitor was deemed to be unreliable in two patients in whom visual but no audio signals were displayed. The audio failure may be attributed in part to an inadequate gain setting in these patients. Negative comments concerned the relatively short duration (5 hours) of battery power available when the bar-graph is used. This problem can be overcome by disabling the bar-graph, and relying only on the audible indication of respiration. The monitor can be used for approximately 50 hours when only audio indicator is in use.

We would like to acknowledge the help of the anaesthetists who participated in the evaluation of the breath monitor, especially Dr D. Shulman.

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Information processing during general anaesthesia

We read with interest Dr Migály's letter (*Anaesthesia* 1990; **45:** 58–9) on 'intra-operative hearing' under general anaesthesia. This is a topic which is receiving growing attention.[1] We must make a few comments although we fully agree with the gist of the letter.

Our original study on the effect of positive suggestions was published as a preliminary version.[2] However, we analysed our data again and published the results.[3] Your correspondent presumed that these were independent studies. The Boeke *et al.* study[4] was indeed based on a new sample with a different method. With regard to this latter study, Migály notes that all patients were administered seaside sounds, as filler sounds, amongst other stimuli. This is correct, inasmuch as the immediate pre- and post-operative phases are concerned, because all patients were thus prevented from hearing possibly disturbing conversation and sounds whilst not yet, or no longer (fully) unconscious.

When anaesthesia was considered during the actual operation to be at a level 'deep' enough to allow surgery to be performed, the four groups differed in the kind of stimuli administered (positive suggestions, nonsense suggestions, seaside sounds, or operating room sounds). One of the four groups of patients (who 'heard' the actual operating room sounds) received no seaside sounds in the experimental phase.

Therefore, this group can hardly be expected to have gained much from the advantages brought about by an evoked right hemisphere dominance. Yet its outcome scores were no less favourable than those of the other groups.

The results of a second replication of the original study, now in progress, in which the same filler sound is used, may reveal more of the possible effects of evoked right hemisphere dominance.

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Acute versus chronic phenytoin therapy and neuromuscular blockade

We read with great interest the study by Gray *et al.* (*Anaesthesia* 1989; **44:** 379–81) on the interaction of acute phenytoin administration with neuromuscular blockade from vecuronium. We were recently alerted to this potential drug interaction when we noticed an apparent sensitivity to vecuronium in a patient who had phenytoin acutely. There was no other reason apparent for increased or prolonged response to vecuronium. We were especially impressed on review of the literature that clinical studies in patients chronically taking phenytoin clearly showed the *opposite* effect: a resistance to the neuromuscular blockade from vecuronium,[1] as well as other non-depolarising agents.[2,3] When, in animal studies, phenytoin was administered acutely, blockade after tubocurarine was potentiated.[4] The article by Gray represents the first data in humans on the interaction of vecuronium with *acutely* administered phenytoin, and sheds important light on this interesting paradox.

We disagree that this interaction is unlikely to be clinically significant. One might expect that vecuronium doses in patients who have phenytoin acutely would be similar to doses for patients chronically receiving phenytoin with Gray's data. Chronic phenytoin leads to vecuronium resistance (compared to no phenytoin),[2] and acute administra-

tion of phenytoin leads to vecuronium sensitivity, so the potential for overdose of vecuronium in patients who receive phenytoin acutely seems very real.

Eight patients for craniotomy were compared retrospectively and were on long-term treatment with phenytoin. Three received phenytoin acutely within 8 hours of surgery. All the patients were treated in a 3-week period. There was no evidence of liver or renal disease and all were extubated in the operating room. All the patients in the chronic group had been taking phenytoin for more than 2 weeks. Review of records revealed slight differences in anaesthetic technique, vecuronium dosing regimen, and criteria for repeat doses of vecuronium. We could thus only hope for a crude comparison of the two groups. We chose to reduce the data for a given patient to total dose of vecuronium per kilogram, per total time from induction to extubation. The average dose was 0.155 (mg/kg)/hour, (SE 0.018) for the chronic phenytoin group. The average dose was 0.0615 (mg/kg)/hour, (SE 0.0079) for the acute phenytoin group. The groups are significantly different, $p < 0.001$ by Student's *t*-test.

Ornstein *et al.*[1] suggested an hypothesis that chronic phenytoin therapy might lead to antagonism of acetylcholine at prejunctional receptors, to induce, in effect, a chronic chemical denervation. This would explain the resistance to non-depolarising relaxants which they reported in patients on long-term phenytoin. A corollary of this hypothesis would be that acute administration of phenytoin should potentiate non-depolarising blockade, as demonstrated by Gray *et al.*

Animal models also predict that twitch tension from direct muscle stimulation should be increased by acute phenytoin therapy.[5] We observed in several cases what appeared to be an exaggerated response to direct stimulation. Failure to delineate such activity from post-tetanic facilitation could easily lead to overdose of muscle relaxant.

Recent initiation of phenytoin therapy in neurosurgical patients is becoming more common, although it was rarely encountered previously. The trend is currently to operate early for intracranial aneurysms. It is therefore becoming more common to bring these patients to operation shortly after emergency admission for subarachnoid hemorrhage. Neurosurgeons frequently give a phenytoin load within 8 hours of operation, or request phenytoin to be given intravenously during the operation, to prevent postoperative seizure. Overdose of muscle relaxant with need for postoperative mechanical ventilation of the lungs represents a potentially serious problem for these patients.

The study by Gray *et al.* adds further emphasis to the wide variability of responses to neuromuscular blockade in neurosurgical patients, and the importance of carefully interpreted monitoring of neuromuscular function.

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A complication of tumour of the oesophagus

This is a report of an oesophageal neoplasm which caused ventilatory insufficiency during anaesthesia.

A 9-year-old boy was to have a modified Heller's cardiomyotomy for suspected achalasia. The child also had a congenital cataract and was deaf. There were no respiratory complaints. He weighed 25 kg and was suitable for general anaesthesia. He was well prepared with oesophageal toilet for 3 consecutive days before operation. A nasoesophageal tube was left in place to keep the oesophagus decompressed. He was given morphine sulphate (5 mg) and promethazine (12.5 mg) an hour before operation. Anaesthesia was induced after pre-oxygenation, with thiopentone (125 mg); suxamethonium chloride (25 mg) was given intravenously and the patient's lungs were ventilated with 100% oxygen. There was acute resistance to ventilation at this stage. Tracheal intubation was with a 6.5-mm red rubber tracheal tube without any difficulty. Anaesthesia was maintained with nitrous oxide, oxygen, and pancuronium bromide (2 mg). However, manual ventilation using the reservoir bag was found to be almost impossible. Breath sounds were markedly diminished on either side. Kinked tracheal tube and bronchial intubation were eliminated, so it was assumed that bronchospasm was the cause. Bronchodilators and corticosteroids were of no avail, so the administration of anaesthetic agents was stopped and the patient ventilated with 100% oxygen. Gradually his spontaneous ventilatory effort returned. Atropine sulphate (0.6 mg) and neostigmine (1.25 mg) were given. The child became fully conscious with adequate spontaneous ventilation and stable haemodynamic status. His lungs were clinically clear and aeration was normal.

Surgery was planned once again a week later. Identical premedication was administered. Anaesthesia was induced with nitrous oxide, oxygen and halothane. Yet again, the administration of suxamethonium was followed by difficulty with ventilation. A 6.5-mm cuffed PVC tracheal tube was inserted and anaesthesia maintained with nitrous oxide, oxygen and pancuronium bromide. The airway resistance worsened; the patient could not be ventilated at all for nearly 30 seconds and cyanosis developed. The ventilation suddenly eased for about 3–4 (positive pressure) breaths, to be followed again by enhanced resistance. This phenomenon of alternating free and obstructed ventilation kept recurring. All the valves in the system, tubes and connexions were checked for malfunction. The PVC tracheal tube was replaced by a 6-mm cuffed flexometallic tube because it was possible that the inflated cuff obstructed the lumen. The problems, however, persisted. We suspected at this stage that the dilated proximal oesophagus could be responsible for the airway obstruction.

Fig. 1. Barium swallow showing lower oesophageal narrowing with enormous proximal dilatation of the oesophagus with no discernible mass in the lower chest.

The patient was therefore turned into the right lateral position. The ventilation immediately became easy and the patient stabilised. A left thoracotomy revealed, to our great surprise, a solid, smooth, spherical tumour about 10-cm in diameter which arose from the lower half of the oesophagus and extended across the hiatus. The proximal oesophagus, including a part of it under the mass, was markedly dilated. The tumour was excised without breach of the lumen. The operative procedure was well tolerated and there was no further difficulty in ventilation even in the supine posture. The reversal from anaesthesia was uneventful. The tumour was a leiomyoma on histological examination.

Airway obstruction is a frightening experience which demands prompt recognition and treatment.[1–6] Acute respiratory distress due to upper airway compression caused by massive proximal dilatation of the oesophagus is a rare complication of achalasia;[7–9] fewer than 10 cases are documented. Proximal airway obstruction makes tracheal intubation difficult and oesophageal decompression affords relief.[9]

There was enormous dilatation of the proximal oesophagus in our patient, which suggested achalasia cardia on X ray (Fig. 1). The presence of a space-occupying lesion was never suspected. However, the patient had no respiratory distress in the awake state and tracheal intubation was easy. It appears, therefore, that the dilated oesophagus had no role in the increase of airway resistance.

Hall and Friedman[10] reported a case of anterior mediastinal tumour in which the induction alone produced profound hypoxia as a result of compression of the pulmonary artery. Decreased muscle tone and an altered intrathoracic pressure pattern during anaesthesia were suggested as causative. Skeletal muscle relaxation helped unmask an abnormality in the thoracic inlet in another case.[6]

We wonder whether a similar explanation is possible in our case. Is it possible, as an alternative that the positive pressure ventilation delivered through the mask or tracheal tube produced pulmonary hyperinflation greatly in excess of that to which the child was used: thereby the tumour was pushed against the membraneous posterior wall at the tracheobronchial bifurcation? The intermittent relief in airway resistance could perhaps be attributed to occasional skidding of the smooth surface of the tumour over the cartilaginous support of the airways. The mass probably fell away from the midline so that the compression became insufficient to produce effective occlusion of the airways when the lateral posture was assumed.

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Craniotomy drains and bradycardias

Drs Joshi, Green and Stedman (*Anaesthesia* 1990; **45:** 169–70) have drawn attention to the occurrence of bradycardia associated with the application of vacuum suction to extradural drains. Many neuroanaesthetists are already familiar with this phenomenon, although it is not widely reported. Bradycardia and asystole may not, however, be due to the generation of a subatmospheric intracranial pressure as illustrated in two accounts below.

A bone flap in one patient was replaced and two drains were sited extracranially below the epicranial aponeurosis after an uncomplicated frontal craniotomy for evacuation of a pituitary fossa haematoma. These were connected to

prevacuumed wound drainage systems (Arthrodax Surgical Ltd., Ross-on-Wye) during closure of the wound. Asystole occurred immediately after the drains were unclamped. The drains were disconnected and atropine 1.2 mg administered intravenously. Sinus rhythm was restored after 20 seconds and the surgical procedure was completed uneventfully.

The second patient was a woman of 44 years who had undergone a frontal craniotomy for clipping of an anterior communicating artery aneurysm. A similar prevacuumed drain was inserted to lie extracranially after closure of the bone flap. The skin was closed and the vacuum applied to the drain. The heart rate decreased from 75 to 43 breaths/minute in nodal rhythm. This was associated with a decrease in blood pressure from 130 mmHg systolic to 100 mmHg. Nothing was done because of the nature of the operation, and after about 30 seconds, the cardiac variables returned to their previous levels. The force of the vacuum was such that the outline of the drain was clearly visible subcutaneously.

The trigeminocardiac reflex, characterised by bradycardia and occasionally ventricular extrasystoles, was described during traction on ocular muscles, manipulation of the maxilla during osteotomy,[1] elevation of zygomatic fractures[2] and direct stimulation of the trigeminal ganglion.[3] A similar mechanism could account for the asystole and the bradycardia in the two patients described since the drains were located within the territory of the ophthalmic division of the trigeminal nerve. The dura is also innervated by the trigeminal and the vagus nerves and, as such, traction caused by application of suction intracranially but extradurally would cause a similar response to that reported by other authors. We believe that this is the most likely explanation for their observations. The introduction of anaesthetic agents devoid of parasympatholytic or sympathomimetic effects, together with a reduction in the use of anticholinergics may be responsible for unmasking these effects.

The trigeminocardiac reflex may represent an expression in man of the primitive diving reflex.[4] This reflex is characterised by bradycardia and apnoea in response to immersion of the face in water. Section of the trigeminal nerve in ducks prevents bradycardia when they dive in the water.[5]

Prevacuumed wound drainage systems used in this hospital generate subatmospheric pressures of 600–700 mmHg. Attempts to provoke this trigeminocardiac reflex by applying similar levels of suction to one of the authors' forehead resulted in considerable bruising, but no bradycardia!

Subatmospheric pressures should be applied to intracranial drains with great caution, if at all. The use of wall suction units does allow the pressure to which the patient is subjected to be measured and controlled unlike the use of prevacuumed systems.

It is important that our neurosurgical colleagues appreciate this problem. If prevacuumed drains are considered to be essential, the anaesthetist must be informed when they are connected and monitoring must certainly be continued into this period; this is already standard practice in some neurosurgical units. Surgeons should be aware of the pressure applied to tissues by these drainage systems.

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Declaration of Helsinki

Dr Drummond comments on appropriate ethical standards in medical research (*Anaesthesia* 1990; **45:** 59) and I fully support his view. The report by Böhrer *et al.* (*Anaesthesia* 1990; **45:** 18–21) raises a related problem: that of an investigation in man that is not considered to be based on reasonable anaesthetic practice.

These authors studied the tussive effect of fentanyl and injected 7 μg/kg fentanyl over one second through a central venous catheter. Sensible anaesthetic practice is to give all drugs slowly and carefully.

There is no obvious benefit to patients in this procedure and I question the ethics of the study and the value of its publication.

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A reply

We completely agree with Dr Grummitt that sensible anaesthetic practice is to give all drugs slowly and carefully. However, certain clinical circumstances especially in cardiovascular anaesthesia require rapid bolus doses of drugs in order not to harm the patient.

Anaesthesia for aortocoronary bypass surgery can be based on a high-dose fentanyl induction technique with fentanyl doses up to 100 μg/kg.[1,2] An initial rapid fentanyl bolus of 7 μg/kg proved to be safe in our hands, for cardiac surgical patients with good left ventricular function, provided that it was not combined with a rapid intravenous benzodiazepine bolus.

Our intention was not to change anaesthetic practice, but to report on a clinical observation that we have made during routine fentanyl administration to cardiac surgical patients. Many cardiac anaesthetists feel that it is quick, easy, and rational to give a single large bolus dose of fentanyl, so we consider it inappropriate to question the ethics of our study.

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Continuous brachial plexus blockade

We read with interest the article by Dr Randalls on this subject (*Anaesthesia* 1990; **45:** 143–4). This block was first described by Ansbro in 1946 who used a malleable metal needle introduced through the supraclavicular route, although his technique was not widely used.[1]

We have used the continuous technique via supraclavicular[2] and axillary[3] routes since 1963 and have used plastic cannulae. We are pleased with this technique and hope that it will be more widely used.

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Controlled ventilation of the lungs in the elderly

The paper (*Anaesthesia* 1989; **44:** 953–8) by Cooper, Leigh and Tring was interesting. Some clarification about one point is needed.

We are told that during the course of the study there were 700 emergency laparotomies, of these 11 with an average age of 70 years were admitted to the ITU to be ventilated after ventilatory failure. We are not told what happened to the other 689.

The authors conclude that all patients over the age of 70 after an emergency laparotomy should receive controlled ventilation of the lungs. Is this the policy they follow now? Would they ventilate these extra 689 patients? Our unit would not be able to cope with such additional numbers. Should we have a larger ITU? Should we offer a treatment (ventilation) which is not risk free to a group of patients because 1.6% of them need it?

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A reply

Dr J.H. Cook makes a very good point.

What we actually stated is subtly different from the inference drawn by Dr Cook: '... *the data suggests that,* if morbidity is to be further improved, emergency laparotomy in patients over 70 years should be followed by elective IPPV postoperatively'.

We do not ventilate the lungs of huge numbers of patients as suggested in his letter. Rather, more patients than before in this elderly age group are considered for ventilation, and more are indeed ventilated. Selection is based on age, debility, risk factors in respiratory or cardiovascular systems and the amount of intraperitoneal soiling, that is, clinical judgement is exercised.

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Preventive medicine in association with anaesthesia

Approximately 33% of adult surgical patients are smokers. Smoking-related diseases account for a large fraction of current medical budgets.

The importance of preventive medicine is now well recognised, although anaesthetists have traditionally had only a minor role to play in this respect.

The effects of suggestions made to anaesthetised patients about their recovery have been recorded. If a patient expresses a desire to give up smoking, as determined at my visit before operation, then I make the suggestion to the patient during their general anaesthetic that he or she will have no wish to carry on with the smoking habit.

Follow-up of these patients at approximately one month after their discharge from hospital shows that eight out of 10 patients in a pilot study have neither smoked another cigarette nor expressed a desire for one. Most ex-smokers believe the first month of quitting the habit is the most difficult.

Should not this suggestion become a more popular technique providing of course that the patient has given their informed consent?

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Hyderabad chloroform commission

There is a picture in the essay[1] on the Hyderabad chloroform commissions of the young ruler of Hyderabad, the Nizam (page 219), but no name and no age. How old was he, when Dr Edward Lawrie (1846–1915) the Residency Surgeon of Hyderabad, talked him into paying the expenses of the commissions in 1888 and 1889?

The answers to these questions may interest others who are interested in the history of anaesthesia.

The Nizam of Hyderabad, Mir Mahbud Ali Kâhn became Nizam in 1869 when he was 3 years old, and he was the ruler of the independent state of Hyderabad until his death in 1911. He was the sixth Nizam and was 22 and 23 years old when the commissions took place. The Nizam was considered to be the wealthiest man in the world at that time (the descendants may still be so) so for him to pay the expenses of the commissions was a simple matter.

When the Nizam died in 1911 he was followed by his son Mir Usman Ali Khän Bahâdur Fatch Jung (born 1886 and died 1967). He was addressed as 'His Exalted Highness the Nizam', and became the last of the ruling dynasty, which was founded in 1724.

India reached independence in 1947 and Hyderabad was taken over by the Indian government by force ('Police action') in 1948. The state of Hyderabad was divided in 1955 along linguistic lines and was added to the three states Bombay (later Maharashtra), Mysore (later Karnataka) and Andra Pradesh. The state of Hyderabad disappeared in this way, but the city of Hyderabad became the capital of Andra Pradesh.

The Nizams were all Muslims ruling a state of Hindus with a small minority. Nizam is a Turkish title, meaning 'regulator of the country'; a title given solely to the Hyderabad ruler by the great Mogul Emperor. Mir is an Arabic title, abbreviation of Emir.

The Nizam of Hyderabad became a wellknown 'shadow figure' in the history of anaesthesia by paying for the two commissions. Maybe this is the most important act by which he should be remembered. He now has a name and has become an 'historical person', at least to me.

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An unusual cause of gas pipeline failure

This is, I think, the first reported cause of pipeline failure due to thermal damage.

A new oil-filled heater was fitted to the outpatient theatre in another hospital during the weekend.

The sound of the oxygen pressure failure alarm on the anaesthetic machine could be heard on Monday morning.

It was apparent on examination of the anaesthetic machine that there was a large hole in the flexible oxygen hose which connected the anaesthetic machine to the wall-mounted gas outlet.

The heater was mounted on the wall directly below the gas outlets, and when the timer on the heater had turned it on, the heater had warmed the oxygen hose, which was lying close to the radiator: the hose had then ruptured under the normal pipeline pressure of 400 kPa.

The relevant British Standards,[1] which govern hose specifications, specify the thermal tolerances of the hoses in respect of pressure tolerances at normal room temperatures.

It is not suggested that the standards should be revised to take into account adverse operating conditions, but the lesson of this event is that new equipment for operating rooms should be installed with consultation with users.

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Reference

1. BRITISH STANDARD NUMBER 5682. 1984 (amended 1987) specification for terminal unit hose assemblies and their connectors for use with medical gas pipeline systems.

The identification of the epidural space

Drs Reynolds and Speedy are to be congratulated on their classic paper (*Anaesthesia* 1990; **45:** 120–3). We agree that avoidance of dural damage in the first place is a priority of epidural analgesia; however, to suggest a continuous saline technique to avoid this complication is mystifying. The only case reports in their article which mention epidural technique associated with subdural complications saline was used to identify the epidural space. Surely the logic of this is to suggest that the use of air and not saline is the method of choice. If as the authors suggest, saline delineates spaces better than air, then opening up the potential subdural space would occur more easily with saline. Indeed, Blomberg in his cadaveric studies confirmed that fluid opened up the subdural space easily in 10 of 15 cases.[1]

Why should a continuous rather than an intermittent technique reduce this potential complication? Does the dura really 'blow away' on locating the epidural space? We suspect that any movement of the dura would only be minimal and would be interested to know if there is any evidence of more movement of the dura with the gentle insertion of a few millilitres of saline as compared to the gentle insertion of a few of air.

We consider that versatility of epidural technique is important and are well aware of the many arguments that favour air over saline and *vice versa* in the process of location of the epidural space. It is misleading on the evidence of their article to imply that fewer subdural complications happen after the use of saline, as inferred by the authors in their conclusion.

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1. BLOMBERG RG. The lumbar subdural extraarachnoid space of humans: an anatomical study using spinaloscopy in autopsy cases. *Anesthesia and Analgesia* 1987; **66:** 177–80.

A reply

We thank Dr Robinson and his colleagues for their interest in our article. They are incorrect to state that in no case

that we cited was loss of resistance to air used to detect the epidural space. Air was used in at least three of the reports.[1-3] The most important element of the technique must be to avoid dural damage, and the fact that saline can be used to delineate the subdural space is irrelevant.

Accidental subdural catheter placement is a rare event and we are unaware of any other survey in which partial subdural needle placement was considered as a possible explanation for various minor aberrations of epidural blockade. There can, as yet, therefore be no evidence to show whether saline or air is more likely to result in partial subdural needle placement or subdural blockade. The final sentence of our paper simply attempts to make a reasoned deduction, where statistical evidence is not available, that if the needle is advanced by pressure on the plunger only, its movement halts automatically on entry into the epidural space, and dural damage is therefore likely to be minimised.

The primary aim of any epidural technique must however be to avoid dural *and arachnoid* puncture, graphically termed 'dural tap'. Those who insist on the use of saline for the loss of resistance technique can boast a dural tap rate of less than 0.4%[4-6] during the training of a constant stream of novices. Those who allow the use of air regard a dural tap rate of at least 1% as inevitable while the technique is learnt, and indeed Norris *et al.*[7] admit to 2.6% dural taps among first year anaesthesia residents.

True, careful training of junior staff goes far to minimise the frequency of dural tap but during this process we do not advocate 'versatility' and allow the use of loss of resistance to air'.

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Contamination of scavenging systems

The British Standards Institution specification for Active Anaesthetic Gas Scavenging Systems (BS 6834:1987) specifies (section 3.3.4) a filter located downstream of the air-break device, that is in the direction of waste gas flow. The filter, which should have a pore size of 150 μm and a minimum surface area of 44 sq cm, is not a bacterial filter but has the aim of keeping the pipework and exhaust installation clean and free from obstruction. The standard acknowledges that these filters may constitute a health hazard, and in a note states that 'to minimise the risk of bacterial contamination when changing the filter, a non-reusable type of filter may be used'.

We have recently upgraded our active anaesthetic gas scavenging system to BS 6834:1987, and installed an APC system which incorporates a disposable filter in the flexible hose that connects the receiving unit (air-break) to the socket outlet of the disposal system. The filters from seven anaesthetic rooms and operating theatres were subjected to bacteriological analysis after 2 and 4 weeks' continuous use to assess the extent of bacterial contamination. The results are illustrated in Figure 1.

Overall contamination of the filters was heavier after 4 weeks' use than after 2 weeks' use. However, after only 2 weeks all filters in both anaesthetic rooms and operating

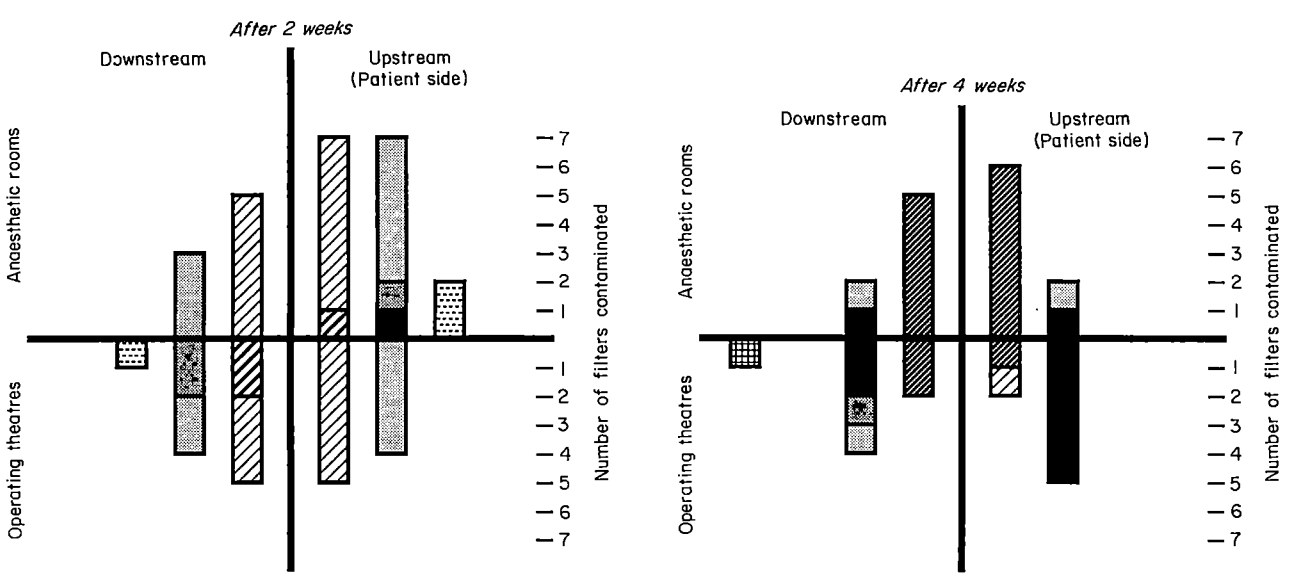

Fig. 1. Contamination of scavenging filters. Bacilli: ▨, light growth; ▨, moderate growth; ▨, heavy growth. Cocci: ▨, light growth; ▨, moderate growth; ■, heavy growth. Respiratory flora: ▨, light growth. Coliforms: ▨, light growth.

theatres were contaminated. The large quantities of bacillus species found in the filters are likely to originate from dust. The gram-positive cocci, which were mostly staphylococci, may have derived either from dust or directly from patients. The respiratory flora and coliforms found are certain to have originated from patients.

A recommendation in Appendix E of BS 6834:1987 suggests that filters are inspected 'daily/weekly... and cleaned or replaced if necessary'. Our results suggest that regular cleaning or replacement should be conducted at intervals of less than 2 weeks. We suggest, in view of the extensive contamination of the filters, that a disposable filter be used. This would provide substantially more protection against bacterial contamination of the maintenance personnel than the use of a reusable filter which requires to be handled during cleaning and sterilisation.

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Closed system use of isoflurane and enflurane

Drs Lawler and Tarpey considered the increased costs of the volatile agents isoflurane and enflurane (*Anaesthesia* 1989; **44:** 596–9). Weis and Englehardt[1] also questioned the proclaimed advantages of these agents over halothane.

Reduction in costs of volatile agent usage, as well as reduction in environmental pollution by chlorofluorocarbons (CFCs), would be achieved if those practitioners with the available equipment would use low-flow circle anaesthesia. The unequivocal safety and easy management of this long-standing technique is clearly demonstrable with the advent of oximeters, end-tidal CO_2 monitors, and gas analysers.

The formula in the addendum of their paper depends on the correct assumption that unsaturated vapour occurs in the flow to the patient. Unsaturated vapour, unlike saturated vapour, obeys the gas laws.

The line: $[(MW/SG) \times (MAC/100) \times (FX1000) \times 60]/24$ should be written but omit the 1000, because, although the result is in ml liquid, the units of the gaseous agents are litres. If the printed formula were used, calculation would have shown that 14810 ml liquid halothane were used in 1 hour, not 14.81 ml.

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Reference

1. WEIS K-H, ENGELHARDT W. Is halothane obsolete? Two standards of judgement. *Anaesthesia* 1989; **44:** 97–100.

Drug usage by anaesthetists

Some information was also collected on drug usage during the course of a survey on attitudes of anaesthetists to premedication carried out in late 1988 and early 1989. This information may interest your readers. 4300 questionnaires were sent to a selection of members of the Association of Anaesthetists of Great Britain and Ireland in the United Kingdom. 1925 completed questionnaires were returned.

It is clear (Table 1) that the usage of thiopentone and fentanyl is far greater than any other induction agent and analgesic respectively. The usage of alcuronium by over 20% respondents is surprising.

The most common induction agent for use in day-case surgery patients is propofol.

Over 89% respondents used suxamethonium in adults if the situation demanded it; 63.5% (1223) consider its side-effects significant. It is not thus surprising that 89% would like a short-acting non-depolarising relaxant.

Halothane (35.8%), isoflurane (23.3%) and enflurane (38%) are used as volatile agents. The relatively greater use of enflurane may be because of the consciousness of the cost of isoflurane. However, over 95% anaesthetists would not repeat halothane at short intervals in adults, although nearly 26% would do so in children. The decreasing use of repeated halothane anaesthetics in children may be because of the fear of medicolegal problems in the face of the directives from the Committee of Safety of Medicines. The data about this particular aspect may be unrepresentative of the paediatric anaesthetists since a large number of respondents probably do not practise paediatric anaesthesia, yet may have answered the question. A majority (78.5%) of respondents would prefer to use halothane for inhalational induction in children; enflurane (6.5%), isoflurane (5.1%) and cyclopropane (4.1%) were also chosen. The use of cyclopropane must be because of the rapid induction of anaesthesia attained with it.

Widespread use of thiopentone, fentanyl and the newer relaxants, atracurium and vecuronium, was also reported in the survey of anaesthetic practice (SOAP) published by the Association of Anaesthetists of Great Britain and Ireland in December, 1988, although the percentage of anaesthetists using these drugs was lower in that survey. The Association Survey was, however, based on the experience

Table 1. Overall frequency of the use of various anaesthetic drugs. (Day case use).

Induction agents		Muscle relaxants		Analgesics	
Thiopentone	83.8% (12.1%)	Vecuronium	32.2%	Fentanyl	58.9%
Propofol	9.8% (70.6%)	Atracurium	29.8%	Morphine	13.9%
Methohexitone	3.6% (7.1%)	Alcuronium	20.4%	Alfentanyl	4.2%
Etomidate	1.2% (0.8%)	Pancuronium	10.4%	Pethidine	4.8%
Others	1.6% (9.4%)	Others	7.2%	Others	18.4%

of about 500 anaesthetists during the course of 10 000 consecutive anaesthetic administrations. The present survey showed a relatively greater use of halothane, although in both reports, enflurane was most commonly used.

Nearly all respondents (97.6%) use neostigmine for reversal of residual non-depolarising neuromuscular block. This is perhaps as much due to the nonavailability of a suitable formulation of alternatives such as pyridostigmine and edrophonium as to the safety and reliability of the action of neostigmine.

The use of both sedative and anticholinergic premedicants and the use of anticholinergic drugs at the time of antagonism of the neuromuscular block is being reported separately.

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Bain, Lack, Mera F and circle systems

Drs Willis and Clyburn, and Dr Hill (*Anaesthesia* 1990; **45:** 172) are quite right to draw attention to the potential dangers of using a standard Bain attachment with a circle system. The resistance of the inner tube from a Penlon Bain has already been reported as 5.1 kPa, measured at a steady 30 litres/minute flow of air, which is some 25 times greater than expiratory resistance of 0.2 kPa in the same system.[1] This is equivalent to respiratory obstruction if the inner tube is part of the inspiratory limb. Inspired gases come mainly from the expiratory side of the system and rebreathing is possible. Movement of fresh gas around the system will depend on the supply pressure. This arrangement was used for the earlier report[2] and compared to a complete Bain system which, however, was supplied with what may have been a less than adequate fresh gas flow: rates of at least three times the minute volume have been found to be necessary.[3] No significant change was reported, nor would be expected if both systems were unsatisfactory. Comparison with a totally different system would be preferable. The Lack system (MIE) offers no increased resistance in its inner pathway and is an effective alternative. A co-axial system specifically designed for use in a circle system with spontaneous breathing is the valveless Mera F circuit (Senko Medical Trading Co, Tokyo).

Geometrically, it does not matter whether the inner tube is part of the inspiratory or the expiratory limb of a circle system. The standard Bain happens to have a very narrow inner tube and in practice it matters very much indeed. If the term 'Bain' was used descriptively to indicate inner flow towards and outer flow away from the patient when a co-axial system was employed, it should be stated clearly that this was so.

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An unusual pulse oximeter artifact

We report an error in oximetry arising during elective percutaneous nephrolithotomy. Anaesthesia was induced with thiopentone and fentanyl and maintained with enflurane in 60% nitrous oxide in oxygen. Muscle relaxation was produced with vecuronium and the patient's lungs ventilated to normocarbia. Intra-operative monitoring included ECG, noninvasive blood pressure, inspired oxygen concentration, capnography, ventilator alarm, plethysmography, pulse oximetry and neuromuscular transmission monitoring.

The 'Myotest' was used to provide a train-of-four stimulus to the ulnar nerve 25 minutes after the start of surgery. Unfortunately, after the train-of-four stimuli, the nerve stimulator was inadvertently switched to a continuous 1 Hz stimulation. The resultant finger movement was not noticed immediately since the anaesthetist was administering more muscle relaxant.

Moments later the pulse oximeter alarm was activated and the monitor displayed a saturation of 89%. The plethysmograph wave form had changed dramatically. A rapid assessment of the patient revealed adequate ventilation and no changes in the F_{IO_2}, pulse rate and volume or colour. Closer inspection of the monitor screen revealed that the plethysmograph waveform and ECG were at different frequencies. The waveform displayed resulted from artifact due to sensor movement from the 1 Hz stimulus superimposed upon the normal plethysmograph trace (Fig. 1).

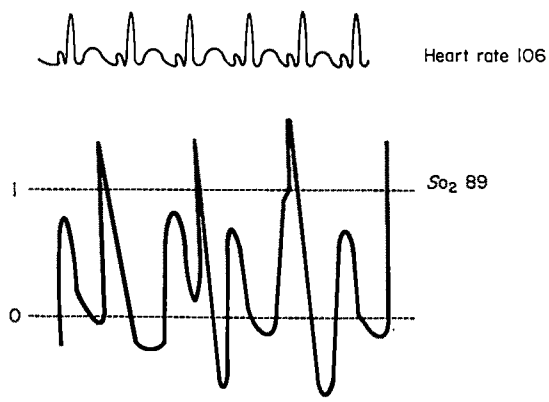

Fig. 1.

This situation is interesting because the patient movement was iatrogenic and resulted in a regular waveform not recognised as interference by the monitor. This source of error may be avoided if the oximeter probe and nerve stimulator are not sited on the same limb.

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P.J. HEATH

Topical lignocaine: ?toxic lignocaine

Drs Luntley and Van Hasselt (*Anaesthesia* 1990; **45:** 61) suggest that lignocaine gel applied to the urethra before catheterisation could have caused hypotension by a direct cardiovascular effect of the absorbed lignocaine. Published work on the absorption of lignocaine from the urethra, however, indicates extremely low plasma concentrations even after quite substantial amounts of the drug are used. Axelsson and co-workers[1] using up to 800 mg (40 ml of 2%) of lignocaine in a gel, obtained mean peak venous plasma concentrations of 0.15 μg/ml, which occurred on average 45 minutes after application. Plasma concentrations were higher in patients who had their urethra dilated, with consequent minor trauma to the epithelium. The mean peak plasma concentration after 400 mg with no dilatation was only 0.06 μg/ml.

These concentrations are thus 1–2 orders of magnitude lower than those which cause mild central nervous system toxicity (5 μg/ml). Cardiovascular effects require even higher concentrations than this.

The cause for the hypotension in their patient must therefore be sought elsewhere. The arterial pressure of 100/80 mmHg seen before the lignocaine is hardly a normal pressure; the small pulse pressure suggests a decreased cardiac output.

If toxicity due to a local anaesthetic is suspected in a patient, it would be helpful to obtain a venous sample at the time, for measurement of the plasma concentration. This would indicate the probable contribution of the local anaesthetic drug to the observed phenomena.

Topically applied, local anaesthetics have a generous safety margin with the exception of spraying down the bronchial tree, when of course the drug can reach the pulmonary capillaries and be absorbed rapidly, particularly in paralysed patients who cannot cough.[2]

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Propofol and lignocaine in children

We were interested to read the letter by Dr Morton about the use of propofol mixed with lignocaine to abolish the pain on injection in children (*Anaesthesia* 1990; **45:** 70). May we point out that propofol is neither yet licensed for paediatric use in the UK nor does Imperial Chemical Industries currently make any recommendations about the mixture of propofol with lignocaine. However, ICI are applying for an extension to the currently approved use of Diprivan and have submitted data on paediatric use and compatibility with lignocaine to the Regulatory Authority.

Finally, may we remind users that propofol is formulated in a lipid emulsion and each 20-ml ampoule is intended for single patient use. Any drug remaining should be discarded and not stored for further use: this avoids the possibility of cross-contamination.

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Sticky labels to indicate hazard for anaesthesia

We have experience with a similar system to that of Bray and Fletcher (*Anaesthesia* 1989; **44:** 938) for 6 years. We printed our own stickers which read: ***ANAESTHESIA ALERT*** *PLEASE CONTACT ANAESTHETIC DEPARTMENT BEFORE BOOKING SURGERY/ ANAESTHESIA.*

This sticker is placed on the front cover of the patient's notes. Simultaneously an entry is made in our departmental Register of anaesthetic-related problems. This comprises a form with details of the patient, the disease, the problem, management of the problem, the outcome and necessity for follow-up, such as further investigation or counsel for the patient or family.

Guidelines for patients to be included are: any complicated anaesthetic which may recur; medical/surgical problems with potential for anaesthetic complications.

The objectives of this register are: to identify patients with possible recurrent anaesthetic problems and their management; to aid future anaesthetics of a particular patient or a patient with a similar problem; and to obtain statistics of the incidence of anaesthetic problems and their management.

The information from this register has been entered into a computerised database. A gross analysis of the six-year period (1984–1989) reveals: 34, difficult intubations; 17, airway problems; 12, suxamethonium apnoeas; 4, malignant hyperthermia; 2, muscular weakness; and 17, miscellaneous events.

These figures are not truly representative of the incidence of problems in our paediatric anaesthetic population of 9000 annually since unfortunately not all eligible patients have been entered into the register. However, the system is working well and has given advance warning of problems.

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Anaesthesia, 1990, Volume 45, pages 503–505

Book reviews

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Recent advances in anaesthesia and analgesia, 16

Edited by R.S. ATKINSON AND A.P. ADAMS. Pp. viii+215. Churchill Livingstone, 1989. £16.50.

The 16th volume of this admirable series has maintained its usual high standard, the editors having chosen an interesting and varied selection of topics. The majority of chapters are clinically based, but with sufficient physiology, pharmacology and physics to appeal to the candidate for higher examinations. Eleven chapters encompass alveolar physiology, nitrous oxide, drug infusions, local analgesia, sedation, fluid therapy, trauma, craniofacial surgery, capnography, pulse oximetry, neuromuscular blockade monitoring and chronic neuropathic pain. Almost every chapter carries at least 50 references, some over 100. The index is adequate, and there are 27 figures, six photographs, and a dozen tables.

Readers are likely to be selective, according to their anaesthetic practice or examination requirements. Forced into the discipline of having to read every chapter, this reviewer found unexpected gems. The chapter on the theoretical and practical aspects of continuous drug infusions, a formidable subject, is excellent. There is little in the anaesthetic literature on craniofacial surgery, so this chapter is recommended, even to nonspecialists, not only for information on these disorders, but for hints on general management, applicable to any infant.

The section on fluid therapy provides a useful reminder of body fluid compartments, clinical and haemodynamic assessment of vascular volume, and the distribution of different types of fluid given intravenously. Occasionally, in order to achieve a broad perspective, depth of discussion has been sacrificed. For example, with reference to treatment of glycine absorption syndrome, the author baldly states that 'an osmotic diuretic to encourage water excretion together with a hypernatraemic solution to replace sodium, would be suitable'. Not everyone would agree that such aggressive treatment is either necessary, or entirely free of complications.

The chapter on local analgesia is of interest, and contains many references to newer modifications of standard techniques. Somewhat surprisingly, interpleural analgesia does not feature, although it is mentioned in the chapter on trauma. It is presumably no accident that the subsequent chapter is devoted to sedation techniques. A wide range of circumstances in which sedation might be used is covered, and anyone administering sedative drugs would benefit from reading this organised and well-referenced chapter.

Dramatic improvements and innovations in patient monitoring have occurred in the last 25 years. Thus, a time when safety is the watchword and minimal monitoring standards in anaesthesia are under scrutiny, reviews on capnography, pulse oximetry and neuromuscular blockade monitoring are apposite.

Chronic neuropathic pain constitutes one of the more difficult therapeutic problems. Thus the interesting theoretical discussion of the cellular and neural effects of aminoglycosides at the beginning of this chapter hinted at an exciting breakthrough in treatment. Disappointingly, little clinical experience of aminoglycoside injections for chronic pain existed at the time of writing. Perhaps this chapter has appeared a little prematurely. Whether this volume is used for examination purposes, as a source of recent references, or for a little light bedtime reading, it is a worthy addition to the anaesthetic bookshelf.

R.A. MASON

Lectures on anesthetics and on asphyxia

CLAUDE BERNARD, translated by B.R. FINK. Pp. xvii+404. Wood Library-Museum of Anesthesiology, USA, 1989. £18.75.

Claude Bernard is rightly regarded as one of the fathers of modern scientific physiology. This translation of his lectures by Dr Raymond Fink shows that Bernard can also lay claim to an influential role in the development of anaesthesia. The volume comprises two series of lectures, the first 10 on anaesthesia and a further eight on asphyxia and concludes with a general lecture on the 'Phenomena of life'. The lectures were given to students and others at the College de France from 1869 to his death in 1878 and were published in 1875 and 1878.

These lectures were given barely 20 years after the introduction of anaesthesia when the mode and site of action and the distinction between anaesthesia and asphyxia was still unclear. Bernard expounded the value of careful observation of human and animal responses coupled with thoughtfully planned experimentation as a means of elucidating these facts. He describes his 'methods and investigative procedures' as the 'rock-solid foundation on which all medical science must be based'. Opponents of vivisection would be horrified at the experiments performed but none can deny their fundamental importance to our present understanding of anaesthesia and physiology; for example, a series of experiments on frogs clearly demonstrated that chloroform's site of action is the brain. Subsequent lectures deal with the value of opioids as premedicants aiding induction and facilitating maintenance of anaesthesia. The studies must constitute one of the earliest investigations of balanced anaesthesia in animals and man. Almost in passing, the intratracheal administration of drugs for rapid action, the ability of opioids to sedate and the necessity for artificial ventilation with curare are introduced to the audience.

The second series of lectures is entitled 'Asphyxia' but is a careful series of studies on the effects of fumes from coal,

predominantly carbon monoxide. I found this less interesting than the previous section but it is nevertheless an object lesson in observation and planning and illustrates Bernard's clear analytical thought. The practical value of this work is seen in the appendix on the dangers of wood burning stoves.

The final lecture sets out the thesis that common features of protoplasm, be it animal or vegetable, are irritability and motility. It goes on to illustrate the thesis with a series of experiments with anaesthetics on animals and plants and concludes that 'an anaesthetic agent ... always acts on irritability and nothing else'.

The quality of the translation is beyond reproach and Dr Fink is to be congratulated in bringing these important documents to a wider audience. The prose conveys the evident excitement and enthusiasm of Bernard for his work while retaining the precision of his thought. The book is modestly priced and can be recommended both to individuals and department libraries. Those who are contemplating a career in research would benefit especially from a careful reading.

C.D. HANNING

Medicine for anaesthetists

Edited by M.D. VICKERS AND R.M. JONES. Pp. vii+600. Blackwell Scientific, 1989. £57.50.

No book which has run into three editions in 12 years can be considered unsuccessful. This new edition of *Medicine for anaesthetists* sees the arrival of R.M. Jones as one editor. The material has been extensively updated, younger authors have been recruited and attempts made to correct 'imbalances' and provide a more correct emphasis on what might be regarded as those parts of medicine most pertinent to the practice of anaesthesia. It is a considerable improvement on the previous edition, and not merely because it is much more up-to-date.

Most of the chapters are the product of combined writing by an anaesthetist and a physician; some, however, are written by anaesthetists alone. The text is generally readable, though perhaps somewhat turgid in places; there are a number of useful tables, mainly for reference, and there are some useful illustrations.

Many, perhaps most, anaesthetists have attempted, when reading for examinations, to use textbooks of medicine with textbooks or monographs on the anaesthetic aspects of the medical problems they are likely to encounter. They need to have a thorough revision of (sometimes grounding in) the practice of elementary clinical examination. They need to be given a sense of proportion in such matters as what investigation may be appropriate in what circumstance, *Medicine for anaesthetists,* though useful background reading (if the student has time), is no substitute for the study of medical texts for examinees in anaesthesia.

Another situation which will send the anaesthetist scurrying to a textbook is the rare condition, carcinoid tumour, phaeochromocytoma, and the like. Here *Medicine for anaesthetists* provides neither quite enough material, nor enough references, to insure good management and the anaesthetist would have to seek out the relevant monograph or article.

Medicine for anaesthetists was a pleasure to read and the reviewer has gained a number of fresh insights into this and that. But it seems to attempt to synthesise for the reader something which perhaps he or she would be better synthesising for themselves.

To the nonspecialist anaesthetist such relatively esoteric tests as pressure/volume loops are of very limited importance. Indeed, most anaesthetists have insufficient background knowledge and experience to make much sense of them. One was left wondering if every trainee would realise that many anaesthetists have passed peaceful and successful lives without ever having made use of such tests.

Editors are in a 'no-win' situation with regard to references. If there are a lot then there are complaints that the text is too broken up and the book becomes longer and more expensive. If there are few then the work is considered over-dogmatic and pedagogic. There is no consistent policy in *Medicine for anaesthetists.* Certainly there are not too many, and the reviewer would have preferred at least some additional up-to-date references on some of the more uncommon conditions described which the anaesthetist might meet. This, as has been implied, limits its value as a reference book. The index, however, seems to be good.

There are the usual number of slips and mistakes to which all texts are prone and in which reviewers tend to exult. The general standard, however, is good. The presentation is attractive and the volume, though not cheap, is at least of manageable size.

J.E. UTTING

Problems in anaesthesia—analysis and management

S. FELDMAN, W. HARROP-GRIFFITHS AND N. HIRSCH. Pp. x+180. Heinemann Medical, 1989. £12.95.

The avowed aim of this slim volume is to encourage the tyro to respond to problems encountered during anaesthesia by 'evaluating the physiological significance of the event and responding appropriately' rather than 'acting in a mechanical, algorithmic fashion'. The authors 'deliberately avoid giving specific criteria for active interference leaving the anaesthetist to make sensible adjustments'. This precis of the preface to the book immediately invites several observations. Is this the correct way to train anaesthetists? When faced with a cyanosed patient or a failed intubation should the learner not be provided with a set of rules (currently called an algorithm) rather than hunt through the vestigial remnants of first degree physiology vainly looking for inspiration? Surely problem solving is all about ingrained algorithms which contain in their construction the necessary background physiology?

Leaving aside these doubts for a moment, does the book fulfil its ambitious aim of teaching a method of problem recognition and solution? The Introduction provides sensible advice on the prevention of problems viz, keep it simple, send for help early but then, that most fatuous of advice, *don't panic!* The book is divided into three sections dealing with respiratory, cardiovascular and miscellaneous problems respectively. Within each section a topic (for example 'difficult airway') is dealt with under the headings: definition, physiological significance diagnosis and management. So far so good. The topics are then treated in a manner that resembles nothing so much as answers to examination questions; 'Discuss the management of the difficult airway'. Some of the answers are very good and some would frankly fail but all, I fear, could have been written by a candidate in Part I of FCAnaes and give very little insight into problem solving.

There is overall discrepancy in style and format, vague, fence-sitting advice in a book which claims to deal with problem management ('some anaesthetists give lignocaine') and much, unquestioning, promulgation of anaesthetic folklore. There is an imbalance in the space given to the problems; drug reactions receive less than three sides of print, problems of one-lung anaesthesia (in a book for novices?) nearly 11 sides.

The diagrams in the book are largely unhelpful; the oxygen dissociation curve appears twice although the shifts mentioned in the text are not illustrated and in a short book there are two pages of a man who models different types of oxygen mask. The 'current' Resuscitation Council's chart is now superseded. The diagrams give the impression of being added as padding as do topics such as haematuria and oliguria in which the time-scale of the problem calls for a different type of approach to its solution. The index is rudimentary.

Throughout medicine there is great interest in the theory and practice of decision-making and problem solving, indeed whole journals are devoted to it. Anaesthesia lends itself to these approaches and works devoted to aims contained in the title of this text are needed. This book fails to live up to the promise of the title and its cost alone would make it an unattractive purchase for its intended readership.

D.A. SAUNDERS

Anaesthesia for uncommon diseases

B.J. POLLARD AND M.J. HARRISON. Pp. viii+271. Blackwell Scientific, 1989. £16.50.

The idea behind this small paperback is good. It is to help formulate a plan of anaesthesia for a patient with an unusual medical, surgical or anaesthetic problem. The method, taking examples culled from the literature, is to highlight major problems and show how they have been dealt with or, in 1989, how they might be dealt with. The idea is good. The result, considering the potential, is disappointing. The uncommon diseases are tabulated but there is little about anaesthetic management.

The book is in essence an alphabetic list of 204 concise but inadequate and lacklustre monographs. The text in about one-third of them occupies less than half a page. The rest of the space is taken up by the name (and synonyms) of the disease (heart block (Stokes–Adams attacks)), a heading (Major problems: sudden cardiac arrest) and, on average, 2.4 references, 40% of which predate *1980*. All but 24 references are taken from the six most popular anaesthetic journals in the English language. Not one of them actually gives the full title of the reference.

Does the text help to formulate a plan of anaesthesia on a pre-operative ward round or after a call for help in the small hours? Let's take hypothyroidism. There are fewer than 100 words of text. Pre-operative clinical diagnosis, especially from the foot of the bed, is notoriously difficult (but vital): 27 words. Peroperative management: 23 words. Post-operative problems: 15 words. There is one reference. What do I do if I am fortunate enough to make the diagnosis (and how do I make it?) during surgery or in the Recovery Room?

Take something rarer. A senior house surgeon is performing an emergency appendicectomy at 0100 hours and I am called in because the patient has 'collapsed'. My intelligent registrar rightly suspects carcinoid syndrome. When I go in to take charge (never having seen a carcinoid crisis) how do I advise my registrar? This book does not tell me. Neither does it cite the classical review article by Mason and Steane nor derive the lessons to be learnt from it.

When I consider what this book should have been and could have been, and the amount of effort clearly put into it, I am more inclined to blame the publishers than the authors. To find a good idea, to write the book (very hard work), and to get it published is almost a miracle. To review the result in such negative terms is a sadness.

P.V. SCOTT

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We thank the publishers for the following books, some of which may be reviewed in future issues of *Anaesthesia*.

Ostlere & Bryce-Smith's anaesthetics for medical students, 10th edn.
T.B. BOULTON AND C.E. BLOGG. Pp. x+271. Churchill Livingstone, 1990.

Manual of pediatric anesthesia, 3rd edn.
D.J. STEWARD. Pp. xiii+445. Churchill Livingstone, 1990. £22.50.

Anesthesia for vascular surgery.
Edited by M.F. ROIZEN. Pp. xvii+505. Churchill Livingstone, 1989. £55.

Norris and Campbell's anaesthetics, resuscitation and intensive care, 7th edn.
D. CAMPBELL AND A.A. SPENCE. Pp. xi+254. Churchill Livingstone, 1990. £9.50.

Clinical cases in anesthesia.
A.P. REED AND J.A. KAPLAN. Pp. 376. Churchill Livingstone, 1990. £22.50.

Anesthesia in emergency medicine.
Edited by G.S. VANSTRUM. Pp. 423. Little, Brown, 1989. £34.

Regional anesthesia: an illustrated procedural guide.
M.F. MULROY. Pp. 277. Little, Brown, 1989. £29.95.

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C. O'NEILL. Pp. 104. S.B. Publications, 1989, distributed by Macmillan. £5.95.

Anaesthesia, 1990, Volume 45, pages 506–523

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for November 1989. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

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The collator of this section is Dr L. Kaufman, MD, FFARCS, 145 Harley Street, London W1N 2DE. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase II, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

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Anaesthesia, 1990, Volume 45, page 524

Safety Action Bulletin (No 56)

Blood administration sets with flexible drip chambers. (90 (10))

There is a potential for disconnexion during rapid transfusion and a number of incidents have been reported to the Department of Health. All similar incidents should be reported to the Department. Excessive pressures should not be applied to these sets. Some of the reported incidents involve the use of a pressure cuff together with manual pumping and others occurred with hand pumping alone.

ECG patient cables, electrodes and lead wire connexion.

There has been another incident in a hospital in which a baby received third-degree burns as a result of the application of mains voltage across the chest despite the warning (Hazard 88: 24). There are new guidelines for patient cables, ECG electrodes and lead wire connexions. References to the Department of Health Bulletin is recommended.

Hazard Notice

Sage Infusion Pumps, including Travenol 5M1177 Heparin Pumps. (HC Hazard) 90 5).

This Health circular advises immediate withdrawal of *all models of Sage infusion pumps* from clinical use.

Erratum

Anaesthesia, 1990, Volume 45, pages 52–54

Local application of EMLA and glyceryl trinitrate ointment before venepuncture

R. D. Gunawardene and H. T. Davenport

The above authors have asked us to point out that '1. inch of glycerine trinitrate ointment (Percutol) contains 16.6 mg and not 1.1–2 mg as stated in the above article. 1–2 mg is the buccal dose; 8–50 mg is the transdermal dose'.

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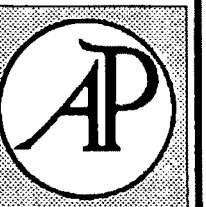

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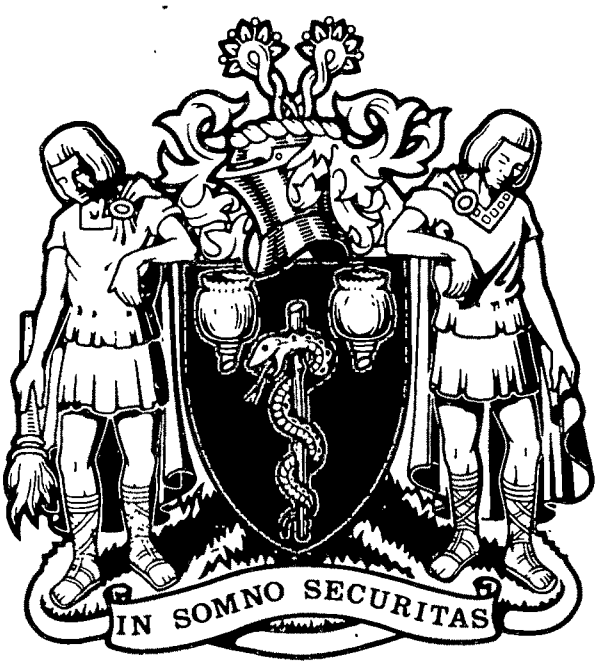

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Awareness under anaesthesia can be a real eye opener

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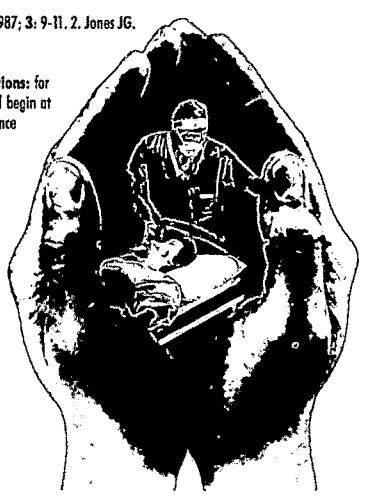

Awareness can occur in patients who are ventilated with nitrous oxide and only given an i.v. agent.[1,2]

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Anaesthesia

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Anaesthesia, 1990, Volume 45, pages 525–526

Editorial

Anaesthesia simulators and training devices

A healthy adult becomes cyanotic and profoundly hypoxaemic (pulse oximeter oxyhaemoglobin saturation < 70%) after induction of general anaesthesia and tracheal intubation. Clear breath sounds are heard bilaterally, and the capnogram demonstrates exhaled carbon dioxide with each ventilatory cycle. The anaesthetist discontinues nitrous oxide and then, despite the continued presence of exhaled CO_2, spends several minutes repeatedly reconfirming that the patient was not accidentally extubated or disconnected from the breathing system, and that oesophageal intubation is not to blame. Pleural catheters are inserted to rule out pneumothorax when elevated airway pressures are noted. The anaesthetist notices, after 6 minutes of profound hypoxaemia, that the oxygen analyser (its audio alarms disabled) displays an inspired oxygen concentration of 4%. Use of the reserve oxygen cylinder fails to improve the F_{IO_2}. Finally, the anaesthesia machine is disconnected from the patient, and the patient's lungs are ventilated with a self inflating bag; the oxyhaemoglobin saturation improves.

This description parallels reports of anaesthesia disasters from contamination of the oxygen supply with another gas. It is one of many very rare but potentially fatal disasters in anaesthesia. Crises like this and malignant hyperpyrexia, cardiac tamponade, venous air embolism, and certain failures of the anaesthesia machine demand a prompt response from the anaesthetist. How can young anaesthetists learn to recognise and correct these rare events rapidly?

Educators in anaesthesia are confronted with three problems when they teach about rare and potentially fatal problems. First, anaesthetists learn best by active experimentation and other forms of active learning.[1] Yet, when learning about rare complications in anaesthesia, the student is forced to learn passively from lectures and written material. Imagine having read about hypoxic-inspired gas mixtures 10 years ago during your anaesthesia training; would you be able to recognise and remedy such a crisis tomorrow? Second, in the operating room, safety of the patient always takes precedence over education. The instructor must intervene and correct the situation when a complication develops that threatens the patient. Learning is compromised. Third, many complications in anaesthesia, such as an hypoxic inspired gas mixture, occur so rarely that few anaesthetists will have encountered such problems during their training.

Simulators are ideal learning tools when the events are rare, the errors expensive or the reality dangerous.[2] A number of investigators in the United States and Great Britain have begun to use simulators in anaesthesia education. A simulator is a 'machine that attempts to reproduce or represent the exact or nearly exact phenomenon likely to occur in the real world'[3] and, in so doing, creates 'an operating imitation of a real activity.'[4] An anaesthesia simulator, then, looks and feels like the anaesthestists' clinical environment at the head of the operating room table.[5] Components of an anaesthesia simulator include a simulated patient, an anaesthetic delivery system with breathing system and mechanical ventilator, and monitoring instruments. Fluid and medication systems and a simulated surgical field can also be part of an anaesthesia simulator. Anaesthesia training devices, in contrast to simulators, present 'only the necessary training stimuli and practice opportunities appropriate to the trainees' learning level and style.'[3] Training devices are used by the student pilot in aviation, to learn the individual cognitive and psychomotor skills necessary to fly a plane. Then, in a flight simulator, the pilot integrates these skills and rehearses responses to engine failure, rough weather, and other problems.

An educational curriculum, which used anaesthesia simulators and training devices, was recently organised and demonstrated by the Anesthesia Patient Safety Foundation, the Society for Education in Anesthesia, and the U.S. Food and Drug Administration. This particular curriculum helps anaesthetists learn about the uptake and distribution of inhaled anaesthetics.[6] The curriculum comprises physical lung models;[7] interactive, computer-programmed uptake and distribution exercises;[8,9] arrhythmia recognition databases;[10] and anaesthetic case management drills both at the computer terminal[11,12] and in full scale anaesthesia simulators.[13,14] Similar curricula could be developed for many subjects in anaesthesia.

The first anaesthesia simulator, Sim I, was developed in 1969.[15,16] This sophisticated simulator included a life-like mannequin, presented palpable pulses, and responded to injected medications. Sim I was used to help anaesthesia residents learn to intubate the trachea. Despite studies that demonstrated its usefulness in helping anaesthesia trainees learn this skill,[17] enthusiasm for Sim I was short-lived, perhaps because the use of computers in medical education was met with scepticism and because an expensive educational tool was used to teach skills that could be taught in the traditional clinical manner. Still, anaesthesia simulators enable students to practise the basics such as tracheal intubation, with fewer patients suffering from chipped teeth, sore throats, or oesophageal intubations. Certain 'basics' in anaesthesia are actually rather complex (e.g. uptake and distribution, the anaesthesia machine), and simulators can facilitate faster learning with fewer patients at risk from complications.

The current generation of anaesthesia simulators and training devices focuses on problem-solving in anaesthesia, especially the anaesthetist's ability to recognise and respond to critical incidents responsible for morbidity and mortality. Both at the keyboard[11,12] and at the head of the simulated operating table,[13,14] these training devices and simulators challenge the anaesthetist first to diagnose and then to treat critical incidents that occur during a simulated anaesthetic. Instructors comment on the student's performance and then return the student to the point where incorrect decision-making first began. This type of rehearsal, facilitated by the

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anaesthesia simulator, helps the anaesthetist develop a systematic approach to the identification and correction of untoward situations.

Few anaesthetists are engineers and many are overwhelmed by the increasing use of technology in anaesthesia. Some argue that because new technology can distract the anaesthetist from the patient, the technology should be abandoned. An alternative explanation for 'technology distraction' is that our educational efforts have failed to help the anaesthetist understand these monitoring instruments, failed to help the anaesthetist to integrate these devices into clinical practice, and failed to show the many problems that technologically advanced monitoring instruments can detect that clinical examination cannot. Anaesthesia simulators can provide a realistic environment where anaesthetists can learn 'hands on' about the clinical utility of new monitoring instruments.

Consider the anaesthetist who uses capnography for the first time. Learning in the operating room is dangerous because the anaesthetist's attention is drawn away from the patient and towards the capnograph. The anaesthetist, with his (her) back to the patient, observes the capnogram and tries to discern the normal from the abnormal, the safe from the unsafe. An anaesthetist who, in contrast, learns how to interpret capnograms in an anaesthesia simulator will have had repeated exposure to, and extensive practice in, the interpretation of both normal and abnormal capnograms before using the device in clinical practice. The anaesthetist, having mastered the monitor, can remain at the patient's head, needing only to glance at the capnogram to extract the pertinent data.

Anaesthesia simulators and training devices are powerful educational tools because they create an active learning environment, allow learning without risk to patients, and enact rare problems in anaesthesia repeatedly in a realistic environment so that diagnostic and therapeutic skills can be practised. Immediate areas of application for anaesthesia simulators and training devices include: the introduction of the anaesthesia tiro to basic problems such as leaks in the breathing system and basic skills such as tracheal intubation; a challenge to the more advanced trainee with complex failures of equipment or rare pathophysiological reactions to anaesthesia such as malignant hyperpyrexia; and assistance for all anaesthetists to understand the use of new, technologically advanced monitoring instruments and the integration of these devices into their practice. Additional applications are limited only by the enthusiasm and creativity of educators.

Many heroic pilots have humbly stated after a safe landing of a crowded passenger airplane that became disabled during flight by engine failure, structural damage, or onboard fire, that they responded to the crisis 'just as we practise it the flight simulator.' If, while I am receiving anaesthesia, the unidirectional valves on the anaesthesia machine become incompetent or the oxygen supply fails or is contaminated or the mechanical ventilator malfunctions and delivers positive pressure high enough to cause pneumothoraces, I hope my anaesthetist, after delivering me safely to the postanaesthesia care unit, will similarly state that he or she responded to the crisis 'just as we practise it in the anaesthesia simulator.' Our patients expect us to be ready for disasters, and anaesthesia simulators and training devices give us the chance to be so prepared.

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Editorial notices

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Anaesthesia, 1990, Volume 45, pages 527–530

A comparison of the effects of omeprazole and ranitidine on gastric secretion in women undergoing elective Caesarean section

M. C. EWART, G. YAU, T. GIN, C. F. KOTUR AND T. E. OH

Summary

This study compares the efficacy of omeprazole and ranitidine at reducing gastric secretion in obstetric patients. Sixty-five women scheduled to undergo elective Caesarean section under general anaesthesia were randomly allocated to receive either omeprazole 40 mg or ranitidine 150 mg orally at 2200 hours the night before and at 0600 hours on the morning of surgery. Intragastric pH and volume were measured immediately after induction of anaesthesia and on completion of surgery. All patients had gastric aspirates less than 25 ml. None of the omeprazole group had an aspirate of pH less than 3.5. Six patients (19%) in the ranitidine group had aspirates of pH less than 3.5, a significant difference from the omeprazole group ($p < 0.05$). Of these six, two (6%) had aspirates of pH less than 2.5. Hence this study showed that omeprazole was more effective and consistent than ranitidine at maintaining gastric pH greater than 3.5.

Key words

Anaesthesia; obstetric.
Gastrointestinal tract; stomach, pH.

Pulmonary aspiration of acidic gastric contents during induction or recovery from general anaesthesia is an important cause of anaesthetic mortality and morbidity. In 1946 Mendelson described an acid aspiration syndrome in obstetric patients and showed experimentally that when gastric juice was neutralised, little reaction was produced in the lungs of affected rabbits.[1] In 1962, Bannister and Sattilaro[2] suggested that the critical pH for severe lung damage in humans was 2.5 and in 1974 Roberts and Shirley[3] suggested that the critical volume of fluid of pH less than 2.5 was 0.4 ml/kg, about 25 ml in humans. A more recent study on rats has shown pH to be a more important factor than volume in determining mortality.[4]

Current regimens of premedication of patients before elective Caesarean section frequently include the use of ranitidine[5] and Moir[6] has advocated giving 150 mg orally on the evening before and on the morning of surgery, omitting all antacids. Surprisingly, only one obstetric study published has examined the efficacy of this regimen, in as few as eight patients.[7]

Omeprazole is a substituted benzimidazole which selectively blocks the proton pump in the parietal cell, the terminal step in the production of gastric acid. Studies have shown that the drug can produce almost total inhibition of gastric acid secretion[8,9] and it has an accepted place in clinical practice for the treatment of severe reflux oesophagitis and the Zollinger–Ellison syndrome.[10]

It has recently been reported that omeprazole 80 mg, given orally the evening before elective surgery, failed to produce gastric volumes less than 25 ml and pH greater than 2.5 in seven out of 20 obstetric patients at induction of anaesthesia.[11] However, in a preliminary study, 30 patients given omeprazole 40 mg the evening before and on the morning of elective Caesarean section all met the above criteria.[12] Neither study revealed any maternal or fetal side effects; drug levels in umbilical cord blood were all low, Apgar scores were satisfactory and progress in the first week of life was normal.

This investigation compares the effects of omeprazole and ranitidine, taken the night before and on the morning of elective Caesarean section, on gastric acid secretion.

Methods

The protocol was approved by the Research Ethics Committee of the Chinese University Faculty of Medicine and

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written informed consent obtained from the patients who were aware that they had the right to withdraw from the study at any time.

Seventy women scheduled for Caesarean section under general anaesthesia before midday were randomly allocated to receive either omeprazole 40 mg orally or ranitidine 150 mg orally at 2200 hours on the evening before and at 0600 hours on the morning of surgery. The mothers were fasted from midnight but were given 30 ml water with their medication. All the women were healthy with uncomplicated pregnancies of at least 36 weeks' duration. Exclusion criteria included any history or symptoms of acid-related gastrointestinal disease, any drug allergy or abuse, and ingestion within the previous month of drugs known to affect gastric motility or secretion, for example metoclopramide or tricyclic antidepressants. Laboratory investigations included routine pre- and postoperative full blood counts.

All women were transported to the operating theatre in the lateral position and questioned before induction to elicit any unusual symptoms which might indicate an adverse drug reaction. They were then placed in the left lateral tilt position and monitored with ECG, noninvasive blood pressure measurement and pulse oximetry.

At least 3 hours after the second dose of medication and after pre-oxygenation, anaesthesia was induced with thiopentone 4 mg/kg while cricoid pressure was applied. Suxamethonium 1.5 mg/kg was given, after loss of the eyelash reflex, to facilitate tracheal intubation. Anaesthesia was maintained with 50% nitrous oxide in oxygen supplemented by 1% enflurane until delivery of the baby, when nitrous oxide was increased to 70% and enflurane reduced to 0.5%. Muscle relaxation was continued with atracurium 0.5 mg/kg and ventilation controlled to an end-tidal carbon dioxide concentration of 4.0–4.5 kPa. Oxytocin 10 units and morphine 0.2 mg/kg were given at delivery. Enflurane was discontinued at skin closure and 100% oxygen administered at the end of surgery. Atropine 1.2 mg and neostigmine 2.5 mg were given to all patients to reverse residual neuromuscular blockade.

Gastric aspiration was performed after induction of anaesthesia and again on completion of surgery, before reversal. A 16-French gauge Salem sump tube was inserted orally, after tracheal intubation, until the third 10-cm marking (65 cm from the tip) was at the lips, and correct positioning in the stomach was checked by auscultation of injected air. Attempts were made to maximise returned volume by repeated aspirations, using a 50-ml syringe, after the tube had been withdrawn 10 and 20 cm and then re-advanced. Aspiration was also performed at the end of surgery with the patient in the right and left lateral positions. Volumes were measured directly from the 50-ml syringe which was graduated in 1-ml markings. Measurements of pH were made within one hour using a Corning 240 pH meter, calibrated daily at pH 4, 7 and 10 and also using Millipore pH paper. One ml was the minimum volume needed for a pH meter reading, so any smaller aspirates had pH measured by paper alone. The investigator performing the measurements was at all times unaware which drug the patient had received.

All infants were examined at birth by a neonatologist and Apgar scores at 1 and 5 minutes recorded. Subsequent progress, including weight gain and suckling ability, was reviewed daily until discharge. Mothers were questioned again postoperatively for any unusual symptoms.

Table 1. Clinical data. Values are expressed as mean (SD).

	Omeprazole	Ranitidine
Age, years	31.2 (4.4)	30.6 (4.6)
Weight, kg	65.2 (7.7)	65.8 (10.3)
Height, cm	156 (4.7)	155 (6.1)
Gestation, weeks	38.3 (0.9)	38.5 (1.1)
Duration of anaesthesia, minutes	53 (14)	51 (11)

Differences not significant ($p > 0.05$).

The Fisher exact test was used to compare the number of patients who failed success criteria. Simple linear regression and the paired *t*-test were used to compare the readings from the pH meter with those from the pH paper. The values from the pH meter were taken except when volumes were less than 1 ml, in which case values from the pH paper were used after being corrected by using the linear regression equation of pH meter against pH paper. Arterial blood pressure and heart rate were analysed using repeated measures analysis of variance. Remaining data were compared using the unpaired *t*-test, Mann–Whitney *U* or Pearson correlation test as appropriate, with $p < 0.05$ considered significant.

Results

Seventy patients were recruited for the trial but five were subsequently withdrawn. Of these, two had surgery delayed, one had an emergency section during the night, one was given only 20 mg omeprazole and one drank two glasses of water before operation. Thirty-two patients remained in the omeprazole group and 33 in the ranitidine group. All women were Chinese except for two Europeans (one in each group) and one Vietnamese (in the ranitidine group). Age, weight, height, gestation and duration of anaesthesia were similar for the two groups (Table 1).

Times from the second dose of medication to the first gastric aspiration ranged from 200 to 340 minutes for omeprazole and 190 to 350 minutes for ranitidine. There were five patients in the omeprazole group and four in the ranitidine group from whom it was not possible to aspirate any fluid at induction. Failure to aspirate any fluid was also experienced with three patients in the omeprazole group and one in the ranitidine group at extubation. Sixteen patients had gastric aspirates, at either tracheal intubation or extubation, less than 1 ml; nine of these had received omeprazole and seven ranitidine.

Intragastric volumes and pH are shown in Figures 1 and 2 and Table 2. All patients had measured volumes less than 25 ml. None of the omeprazole group had an aspirate of pH less than 3.5. Six patients (19%) in the ranitidine group had aspirates of pH less than 3.5 ($p < 0.05$). Of these six, two (6%) had pH values less than 2.5. At induction, only one out of the 11 patients with an intragastric pH less than 5 had received omeprazole; at extubation, there was only one out of 14. There was no correlation between intragastric pH or volume and the time from the second dose of medication to aspiration.

Apgar scores and birth weights were similar for the two groups but induction to delivery times were longer in those who received omeprazole (Table 3). Eight babies were admitted to the Intensive Care Unit; from the omeprazole

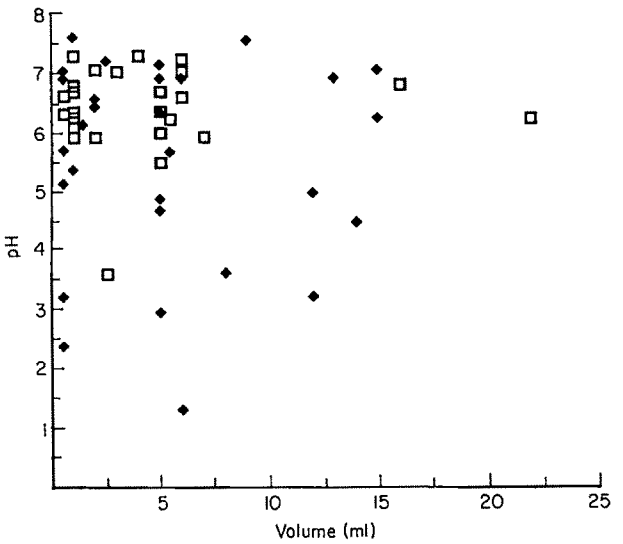

Fig. 1. Intragastric pH and volume immediately after induction of anaesthesia. □, omeprazole group; ◆, ranitidine group.

group there were two sets of twins who required observation due to low birth weight and one baby with a cleft palate who was later diagnosed as having the Tetralogy of Fallot. One baby from each group required observation because of difficulty with delivery and a second baby from the ranitidine group developed neonatal jaundice needing phototherapy.

There were no events which might have indicated an adverse drug reaction. Heart rate, blood pressure, pre- and postoperative haemoglobin concentrations were all similar for the two groups.

Good correlation was obtained between pH meter and paper ($r = 0.973$) but values from the paper were nearly always higher with a mean difference of 0.442 pH units ($p < 0.0001$).

Discussion

Omeprazole is destroyed by acid and is given in enteric coated tablets. It is cleared rapidly from plasma, after absorption from the duodenum, with an elimination half-life of 0.5–1.5 hours.[13] It is a pro-drug only activated at pH less than four and is concentrated in the acidic environment of the parietal cell where it remains for 16–48 hours.[14] Thus the effect on acid secretion does not correlate with plasma levels. Serious side effects have not been reported, possibly because its action is so selective.

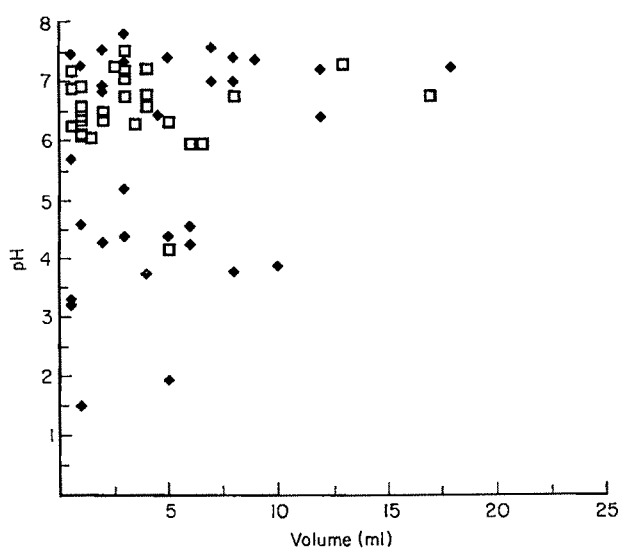

Fig. 2. Intragastric pH and volume on completion of surgery. □, omeprazole group; ◆, ranitidine group.

Table 2. Volumes and pH of gastric aspirates. Values are expressed as median (range).

	Volume (ml)	pH
Omeprazole		
Initial	1.5 (0–22)	6.59 (3.61–7.30)
Final	2.3 (0–17)	6.60 (4.20–7.54)
Ranitidine		
Initial	5.0 (0–15)	6.11 (1.30–7.61)
Final	4.0 (0–18)	6.43 (1.49–7.81)

Differences not significant ($p > 0.05$).

The dosage regimen for ranitidine in this study was advocated for elective Caesarean section[6] and used in previous trials on obstetric[7] and general surgical patients.[15–17] The dose of omeprazole was chosen as a result of the preliminary study carried out at this hospital.[12]

Omeprazole, in comparison to ranitidine, would be expected to produce longer lasting suppression of gastric acid secretion[13] but the enteric coating may cause a delay in absorption and peak effect. There was, however, no correlation between intragastric acidity or volume and the duration from the second dose to aspiration. The six patients with pH values less than 3.5 were induced between 185 and 240 minutes after their second dose of ranitidine, a period of time when that drug should have been working effectively.[16]

Times from induction of anaesthesia to delivery of the baby were greater in those patients who had received omeprazole rather than ranitidine but the reason for this is not clear, it is possibly obstetric in origin.

The usual acceptable criteria for intragastric acidity and volume before general anaesthesia are values above pH 2.5 and below 25 ml. However, pulmonary damage may occur at a pH in excess of 2.5. Pneumonia has been reported in a patient who aspirated material with a pH of 3.5.[18] Respiratory epithelium is damaged in animals after aspiration of gastric contents of pH 5.9[19] and prostaglandin E_2, which is present in gastric fluid, causes tachypnoea and hypoxaemia after aspiration.[20] In addition, the proteolytic enzyme pepsin remains active unless pH exceeds 4.5.[21]

Table 3. Apgar scores, birth weights and induction to delivery times.

	Omeprazole	Ranitidine
Apgar scores, median (range)		
1 minute	9 (6–10)	9 (6–10)
5 minutes	10 (9–10)	10 (9–10)
Birth weight; kg, mean (SD)	3.07 (0.45)	3.22 (0.54)
Induction–delivery; minutes, mean (SD)	15.0* (5.3)	12.5* (3.3)

*$p < 0.05$, other differences not significant.

At present, attempts to reduce intragastric volume and acidity rely on various combinations of H_2 receptor antagonists, antacids and metoclopramide. No ideal therapy has been defined and many different regimens are followed.[5] Antacids are short acting, increase the volume of gastric contents and if particulate may actually cause pneumonitis.[22] A drug capable of reliably reducing intragastric acidity and volume would remove the need to administer antacids in the elective situation.

Blind gastric aspiration may underestimate intragastric volume[23] but this is the common, simple method used in similar trials. Even if one considers that the postoperative aspirate may have been present at the beginning of surgery, the total aspirate volumes are still low with a median (range) of 5 (0–25.5) ml for omeprazole and 8.5 (0–24) ml for ranitidine.

Placental transfer of omeprazole was reported in sheep[24] and humans.[11] In the latter study, neonatal intragastric pH ranged from 6.0 to 8.0 after delivery but subsequent changes in acidity were not evaluated. However, normal intragastric pH at birth is near neutral[25] and omeprazole would not be activated under these conditions.

In conclusion, if one believes that pulmonary damage may occur after aspirating material of pH 3.5[18–21] then the patients given omeprazole in this study were at significantly less risk than those given ranitidine.

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Comparison of epidural sufentanil plus clonidine with sufentanil alone for postoperative pain relief

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Summary

Sufentanil 25 μg plus clonidine 1 μg/kg administered epidurally was compared with epidural sufentanil 50 μg alone in a double-blind fashion for pain relief in 40 patients after abdominal surgery. The duration of complete pain relief was significantly longer in those who received the mixture. Oxygen saturation was reduced 10 and 20 minutes after sufentanil alone, but remained stable after sufentanil and clonidine. There were significant decreases in arterial blood pressure in the latter group that were maximum between 20 and 120 minutes after administration.

Key words

Analgesics, narcotic; sufentanil.
Sympathetic nervous system, alpha adrenergic agonist; clonidine.

Morphine is the longest acting opioid when given epidurally, although it causes the serious disadvantage of delayed respiratory depression.[1,2] In contrast, the lipophilic opioids, such as sufentanil, tend to be associated with early appearance of side effects but a rather limited duration of action. The α_2 adrenoceptor agonist clonidine was shown to produce pain relief when administered intravenously, intrathecally and epidurally,[3,4] and was also shown to potentiate the action of opioids.[5]

The purpose of this present study was to compare the analgesic effects of epidural sufentanil 50 μg with a mixture of sufentanil 25 μg and clonidine 1 μg/kg, and to determine whether the latter mixture would reduce the incidence of the early side effects seen with the larger dose of sufentanil alone.

Methods

The study was approved by the Hospital's Ethics Committee and informed consent was obtained from each patient.

Forty patients scheduled for abdominal surgery were randomly assigned to receive, in a double-blind fashion, either sufentanil 25 μg plus clonidine 1 μg/kg (group 1) or sufentanil 50 μg (group 2) made up to a volume of 10 ml with normal saline. The drugs were given into an epidural catheter inserted at T_{7-8} for upper abdominal and T_{11-12} for lower abdominal surgery. The catheters were inserted before operation but no drugs given until after completion of surgery. General anaesthesia consisted of fentanyl 2–5 μg/kg, thiopentone 3 mg/kg and 50% nitrous oxide in oxygen supplemented by up to 1% enflurane. Muscle relaxation was provided with pancuronium 0.1 mg/kg.

The epidural drugs were given after operation when the patient complained of pain and the pain score on the visual analogue scale was greater than five. Visual analogue pain scores (0–10), arterial blood pressure and heart rate were recorded before drug administration, at 20, 40 and 60 minutes and thereafter hourly until the next injection. Sedation was also scored, in the following manner: 0, none; 1, mild, heavy eyelids, drowsy; 2, moderate, eyes closed, but open with any environmental noise; 3, marked, eyes closed but open on being spoken to; 4, severe, eyes remain closed even when spoken to; 5, comatose and unrousable.

Oxygen saturation (Ohmeda Biox 3700) was displayed continuously. Oxygen, 4 litres/minute via facemask, was only administered when the oxygen saturation decreased below 90%. Respiratory rate was also measured at 20-minute intervals for the first hour and then hourly.

Further analgesia was given when the visual analogue score reached 5, and in all cases consisted of sufentanil 50

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μg. The study was continued for 24 hours after operation and any side effects were noted. The patients were questioned with regard to the quality of analgesia they received.

Results were analysed using analysis of variance for repeated measurements (ANOVA). This was followed where appropriate by the Scheffe test. The Mann–Whitney *U* test was also used for comparisons between the two groups. Values were considered statistically significantly when p was < 0.05.

Results

The groups were comparable with regard to age, weight, sex distribution and type of operation (Table 1).

Details about pain relief in the two groups are shown in Table 2. There was no difference between the times from tracheal extubation and the first epidural injection. Analgesia was experienced within 10 minutes by the majority of patients, but its onset was significantly faster in group 2. The time to complete pain relief (analogue score less than 1) did not differ between the groups, but complete analgesia lasted significantly longer in those who received the sufentanil–clonidine (251 minutes compared to 144 minutes, $p < 0.05$). The pain scores are shown graphically in Figure 1. The only significant difference between the two groups occurred at 120 minutes ($p < 0.05$).

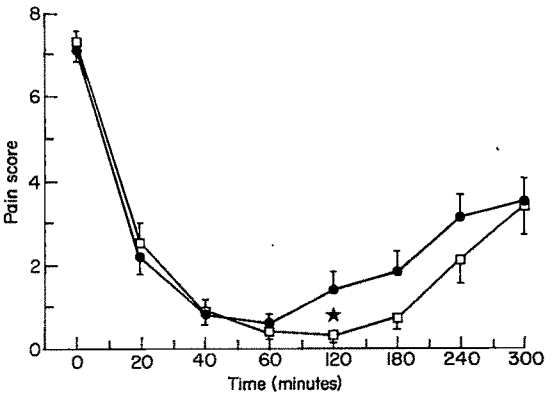

Fig. 1. Linear analogue pain scores during the first 300 minutes, mean (SEM). *p < 0.05. (□—□) sufentanil 25 μg plus clonidine 1.0 μg/kg; (●—●) sufentanil 50 μg.

Table 1. Patient data.

	Group 1	Group 2
Age, years; mean (SEM)	42.5 (3.3)	46.05 (3.6)
Weight, kg; mean (SEM)	68 (2)	69.1 (1.9)
Male/female ratio	7/13	7/13
Type of surgery		
Gastrectomy	2	1
Cholecystectomy	4	6
Laparotomy	4	2
Colorectal	3	3
Gynaecological	7	8

Group 1, sufentanil 25 μg+clonidinel μg/kg.
Group 2, sufentanil 50 μg.
There were no statistical significant differences.

Table 2. Extubation–first dose interval, onset and duration of pain relief of the first and subsequent injections. Values are expressed as minutes (SEM).

	Group 1	Group 2	
Time interval from extubation to first dose	58.0 (6.2)	64.2 (8.3)	ns
Onset	8.8 (1.0)	5.8 (0.9)	$p < 0.01$
Onset to VAS < 1	34.1 (2.8)	35.5 (3.4)	ns
Duration	393.0 (46.3)	321.0 (31.8)	ns
Duration of visual analogue score < 1	251.5 (43.7)	144.2 (27.5)	$p < 0.05$
Duration of the subsequent top-ups	357.0 (32.2)	303.9 (13.9)	ns

ns, not significant.

The oxygen saturations during the first hour after epidural injection are shown in Table 3. Oxygen saturation was significantly lower than control at 10 and 20 minutes in those given sufentanil alone ($p < 0.05$). Thirteen of the 20 patients in this group required oxygen therapy compared to four in those who received sufentanil and clonidine. The respiratory rate decreased to four breaths/minute and the oxygen saturation to less than 70% in one patient who received sufentanil 50 μg; this also occurred after the second sufentanil injection and was easily reversed by naloxone 0.4 mg intravenously. The hypoxia in all instances was reversed by administration of oxygen.

The degree of sedation in the first 3 hours is shown in Figure 2. There was no relationship between sedation and oxygen saturation.

Arterial blood pressure in those who received sufentanil and clonidine was significantly lower than control from 20 minutes to 3 hours (Table 4). Ephedrine was given to four of these patients when the systolic pressure decreased to less than 90 mmHg. A decrease in arterial systolic pressure

Table 3. Oxygen saturation levels, expressed as mean, percent (SEM), and respiratory frequency.

	Time (minutes)				
	0	10	20	40	60
Group 1	94.6 (0.7)	93.4 (0.8)	93.7 (0.8)	92.8 (0.8)	94.6 (0.6)
Breaths/minute (SEM)	15.3 (1.1)	13.1 (0.9)	13.4 (0.8)	14.1 (0.9)	13.9 (1.0)
Number who required oxygen supplementation	2	3	3	4	4
Group 2	95.8 (0.8)	88.9 (1.5)***	92.6 (1.0)*	94.3 (0.8)	93.9 (0.9)
Breaths/minute (SEM)	14.9 (1.0)	13.0 (0.8)	13.2 (0.8)	14.2 (1.1)	14.0 (0.9)
Number who required oxygen supplementation	1	10	13	13	13

*p < 0.05, ***p < 0.001, compared with time zero.

Table 4. Systolic blood pressure values, mmHg (SEM).

	Time (minutes)					
	0	20	40	60	120	180
Group 1	125 (3.3)	110.2*** (2.4)	105.2*** (2.9)	99.9*** (3.0)	102.2*** (2.8)	111.6** (3.2)
Group 2	127.5 (3.5)	123 (3.4)	118.9 (4.3)	119.5 (3.9)	124.7 (3.4)	124.1 (3.3)

**p < 0.01, ***p < 0.001, compared with time zero.

Table 5. Side effects.

	Group 1 (*n*)	Group 2 (*n*)
Spo_2 < 90%	4	13
Systolic blood pressure decrease > 20 mmHg	12	5
Pruritus	1	0
Nausea/vomiting	2	1
Urinary retention	1	3

of greater than 20 mmHg occurred in 12 of these patients compared to five who received sufentanil alone.

Sixteen of the patients who received only sufentanil as their first injection and 14 who received the mixture did not notice any difference in quality of analgesia between their first and second injections (which was always sufentanil alone). Four in each group found the second injection superior, while two who received sufentanil–clonidine experienced better pain relief than with sufentanil alone. There were no differences between onset and duration of pain relief after the second injection.

There was no significant difference between the incidence of pruritus, nausea and vomiting and urinary retention between the two groups (Table 5).

Discussion

Morphine has the longest duration of action when administered epidurally, but the incidence of delayed respiratory depression is such that its use is only acceptable when patients are nursed in a high dependency or intensive care unit postoperatively. The last dose should be administered at least 12 hours before discharge to an ordinary ward. In contrast, the side effects after the more lipophilic opioids tend to occur early, although biphasic respiratory depression has followed epidural sufentanil, but has been ascribed to the residual effects of general anaesthesia, pre-existing pulmonary disease or accumulation from frequent top-ups.[7,8]

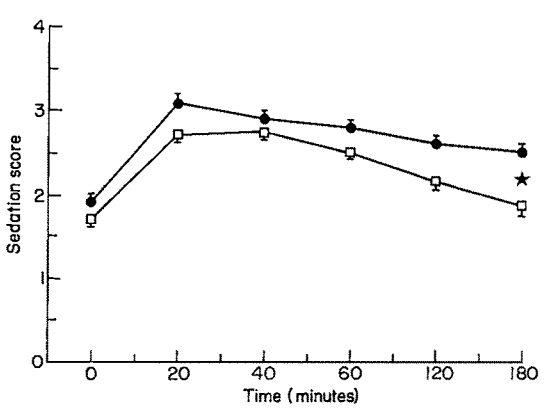

Fig. 2. Sedation scores during the first 300 minutes, mean (SEM). (□—□) sufentanil 25 μg plus clonidine 1 μg/kg; (●—●) sufentanil 50 μg. *p < 0.05.

It is suggested that concomitant administration of naloxone could prevent delayed respiratory depression which results from epidural morphine,[9] but the optimal dose is not defined and combined therapy complicates patient management. Others have suggested that addition of adrenaline reduces the incidence of side effects. However, Bromage *et al.*[10] found that although this prolonged the analgesic effects of epidural morphine in volunteers, it actually increased the incidence of late onset side effects that resulted from an increased amount of drug available for dural penetration and hence rostral spread. Combined with lipophilic drugs, adrenaline might reduce early side effects related to systemic absorption. Several workers have shown a longer duration of action with added adrenaline, but were unable to show a concomitant decrease in plasma levels of the drugs.[11–14] In contrast, Verborgh *et al.*[15] showed both a prolonged effect and significantly lower plasma levels after addition of adrenaline to sufentanil 75 μg.[15]

The dose of the α_2 adrenoceptor agonist, clonidine, to produce effective analgesia varies from 2–4 μg/kg.[16,17] Hypotension is a common complication, especially with the higher dose, and is most pronounced 60–120 minutes after administration, but small doses (75 μg) of clonidine alone epidurally only produces partial pain relief.[18] We found, in a preliminary study, that clonidine 1 μg/kg alone epidurally did not produce effective analgesia and hence a control group that used only clonidine was not thought to be justifiable. A dose of 2 μg/kg was shown to produce satisfactory analgesia for 3–4 hours after orthopaedic and minor perineal surgery.[19] In contrast, clonidine 3 μg/kg epidurally was found to be completely ineffective after thoracotomy.[20]

A synergistic effect was found when opioids were combined with clonidine in the management of terminal pain,[21–23] but the results in the treatment of postoperative pain conflict. Addition of clonidine to local anaesthetics appears to prolong the block.[24] Some workers have found an additive effect when clonidine was combined with opioids,[25,26] but no benefit was found when nalbuphine was combined with clonidine 75 μg compared to nalbuphine alone.

The purpose of our present study was to see if it was possible to reduce the dose of sufentanil by combining it

with clonidine 1 μg/kg and to retain the analgesic effects, but reduce the onset of early side effects associated with epidural sufentanil. The optimum dose of the latter appears to be 50 μg when used alone.[27–30] We have shown that the combination of sufentanil 25 μg with clonidine 1 μg/kg produced longer lasting and better quality pain relief than sufentanil 50 μg alone.

It was also noticeable that oxygenation was not a problem when the lower dose of sufentanil was used. The hypoxia was readily correctable by oxygen administration, but the importance of oxygen therapy and measurement of oxygen saturation in patients who receive epidural opioids must be borne in mind. The main problem associated with the use of epidural clonidine is arterial hypotension, and 25% of patients required active treatment for its correction.

This study has shown a synergistic effect between clonidine and sufentanil when used epidurally in the management of postoperative pain. This has allowed use of a smaller dose of sufentanil, which was associated with a lower incidence of arterial desaturation. Hypotension, however, was a common complication.

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Anaesthesia, 1990, Volume 45, pages 535–537

Evaluation of two formulations of dihydrocodeine using patient-controlled analgesia

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Summary

A randomised, double-blind study of 90 patients after cardiac bypass surgery was undertaken to assess the relative analgesic efficacies of normal- and controlled-release oral dihydrocodeine. Patients received either placebo, normal-release dihydrocodeine, or controlled-release dihydrocodeine at regular intervals on the first to third days after operation. This was supplemented in all groups by intravenous morphine administered on demand by a patient-controlled analgesia system. Morphine requirements in the control group were significantly greater during this 48-hour period than in either of the active groups ($p < 0.01$), but there was no statistically significant difference between the two active preparations.

Key words

Pain; postoperative.
Analgesics; dihydrocodeine.

Dihydrocodeine is a well established opioid analgesic indicated for pain of moderate to severe intensity. It has been available in tablet or injectable form for many years, but a controlled-release oral preparation has recently been developed (DHC Continus tablets, Napp Laboratories) which has the advantage of requiring less frequent administration.

The aim of this study was to assess whether concurrent administration of either form of the drug reduced morphine consumption in the postoperative period when compared with placebo, and whether there was any difference in the analgesic efficacy and clinical duration of effect of the two formulations. Conventional methods of assessing analgesia such as subject or observer observation, linear analogue scales and dose of morphine administered are relatively crude.[1] We chose in this study to measure morphine consumption using patient-controlled analgesia (PCA) which has been shown previously to provide a sensitive measure of analgesic requirements.[2]

Methods

Consecutive patients, aged between 18 and 70 years, who weighed 45–100 kg, and who had undergone elective cardiac bypass surgery were considered suitable. Patients with respiratory insufficiency, hepatic or renal impairment, or those known to abuse alcohol or drugs were excluded. The study had the approval of the Hospital Ethics Committee. All patients were visited before surgery, had the nature of the trial explained, and gave written informed consent. All patients remained sedated at the end of surgery and were transferred to the cardiac intensive care unit. They received intermittent positive pressure ventilation until each patient's cardiovascular variables, blood gas results, temperature, and conscious level were satisfactory. Analgesia was provided with intramuscular papaveretum 10–20 mg 4-hourly as required after weaning from mechanical ventilation; the standard procedure for the intensive care unit.

Patients were reassessed on the morning after surgery. Those who were still unconscious or confused, or who had cardiovascular instability were excluded. Administration of vasoactive drugs was not a reason for withdrawal if the cardiovascular system was stable. Patients, 72 male and 18 female, formally entered the trial after this assessment.

Patients were attached to a Graseby PCAS patient-controlled analgesia system immediately after this assessment, programmed to deliver 1 mg morphine sulphate in response to a button press by the patient. The lock-out period was 3 minutes, which allowed a maximum dosage of

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Table 1. Reasons for exclusion from analysis.

Reason	Number of patients in each group		
	Controlled-release dihydrocodeine	Normal-release dihydrocodeine	Control
Protocol violation	2	4	3
Severe nausea, or vomiting	3	1	1
Extreme drowsiness	1	—	—
Inadequate analgesia	—	1	—
Fatal graft occlusion	—	1	—
Cardiovascular instability and confusion	—	—	1

morphine of 20 mg/hour. In addition, all patients received a continuous background infusion of 0.1 mg/hour to ensure patency of the intravenous line.

Study medication started 2 hours later. Patients were randomised to receive either: controlled-release dihydrocodeine tablets 60 mg 12 hourly; normal-release dihydrocodeine 30 mg 6 hourly; or placebo tablets 6 hourly. Patients in group A received placebo tablets in the intervals between doses so that all patients received tablets 6 hourly. The tablets were identical in appearance and blister-packed to indicate the order in which they should be given. Therapy was continued in all patients for 48 hours. Patient cumulative morphine requirements were recorded over 48 hours and any adverse effects experienced by the patients were also noted.

Demographic data were analysed using Student's *t*-test and Chi-squared tests where appropriate. Administration of opioids in the postoperative period before the start of the trial, and morphine consumption during the trial period were analysed using the Kruskal–Wallis test.

Results

Ninety patients were included in the study. Eighteen were subsequently excluded from the analysis for reasons summarised in Table 1. Most protocol violations were caused by tablets being omitted or given in the wrong order, or where cumulative morphine consumption was not recorded properly. One patient did not receive adequate analgesia because despite prompting, he seemed unable to understand the concept. Another patient occluded several coronary artery bypass grafts, suffered a cardiac arrest, and died during the trial period. There were no significant differences between the groups for age and sex or for the amount of intramuscular papaveretum received in the period between weaning from the ventilator and the start of the study (Table 2). The total morphine consumptions for the 48-hour trial period are shown in Table 3. Both groups who received active agents required significantly less morphine than the control group ($p < 0.01$), but there was no significant difference between those who received the normal release and controlled-release formulations of dihydrocodeine.

The most common side effects were vomiting or nausea (Table 4). These occurred in 11 of 26 patients in group A, four of 25 in group B, and six of 27 in group C. (Totals include patients withdrawn from the trial because of vomiting.) There was no statistically significant difference between the treatment groups. Other adverse effects recorded were wheeze, hallucinations, drowsiness, headache, and heartburn.

Discussion

Examination of the morphine consumption of patients who used patient-controlled analgesia (PCA) was used previously as an unbiased assessment technique to evaluate analgesic drugs.[3–5] It has proven a sensitive technique which can demonstrate variations between different analgesic regimens and between different methods of analgesic administration.[6] We chose to evaluate the different formulations of dihydrocodeine in post-cardiac bypass patients because they receive a standard surgical incision, have a narrow age range and, in our hospital, represent one of the most common surgical procedures undertaken. We have shown in this study that postoperative administration of oral dihydrocodeine reduces morphine requirements in cardiac surgical patients significantly. The new controlled-release formulation of dihydrocodeine given twice daily exhibits a similar morphine-sparing effect to that of stan-

Table 2. Comparisons of groups.

	Controlled-release dihydrocodeine $n = 23$	Normal-release dihydrocodeine $n = 23$	Control $n = 26$
Males : females	16 : 7	17 : 6	24 : 2
Age, years (SD)	57 (7)	55 (8)	55 (8)
Pretrial papaveretum (mg)			
Median	20	15	15
Range	0–60	0–30	0–20

Table 3. Total morphine consumption in 48 hours.

	Controlled-release dihydrocodeine $n = 23$	Normal-release dihydrocodeine $n = 23$	Control $n = 26$
Morphine consumed (mg)			
Median	52.0*	44.1*	62.0
Range	9.4–106.5	16.5–127.3	16.6–144.6

*$p < 0.01$

Table 4. Distribution of reported side effects.

	Number of patients in each group		
	Controlled-release dihydrocodeine	Normal-release dihydrocodeine	Control
Side effect			
Nausea/vomiting	11	4	6
Hallucinations	2	2	2
Drowsiness	3	3	1
Headache	1	1	1
Hiccough	1	—	—
Wheeze	—	—	1
Heartburn	—	—	1

dard release dihydrocodeine given four times daily. In contrast, there appeared to be a higher frequency of nausea and vomiting in patients who received controlled-release dihydrocodeine than in the other two groups, although this was not statistically significant.

In conclusion, we have shown that oral dihydrocodeine significantly reduces the morphine requirements in the early postoperative period using the model of post-cardiac surgery. We thus conclude that it may be a suitable analgesic agent for other patients who experience moderate to severe postoperative pain and whose gastrointestinal function has not been disturbed by surgical intervention. The reduced frequency in dosing of the controlled-release preparation may be an advantage to staff and patients in a busy ward and to patients who have day stay surgery.

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Comparison of intramuscular ketorolac and morphine in pain control after laparotomy

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Summary

Ketorolac, a prostaglandin synthetase-inhibiting analgesic, was compared with morphine for relief of pain after laparotomy for gynaecological surgery. Eighty patients were studied; they were given either ketorolac 30 mg intramuscularly followed by 10 mg 4-hourly as required, or morphine 10 mg intramuscularly 4-hourly as required, administered in a double-blind, randomised fashion. Pain scores (verbal and visual analogue) were recorded at baseline and assessed at 30 and 60 minutes and then hourly for 6 hours. Pain relief was measured at the same times. Pain and pain-relief scores were further assessed on the evening of day 1 and at 24 hours. Pain scores were similar in the two groups but pain-relief scores were better in the morphine group. A considerable number of patients suffered postoperative nausea and vomiting but there was no difference between the groups. One patient in the ketorolac group had unexplained hypotension. It is concluded that ketorolac can provide effective postoperative analgesia.

Key words

Pain; postoperative.
Analgesics; ketorolac, morphine.

Ketorolac trometamol is a nonsteroidal anti-inflammatory analgesic with prostaglandin synthetase-inhibitory properties that have been demonstrated in humans and animal models. A number of studies were conducted in the treatment of postoperative pain using both the oral and intramuscular formulations of ketorolac. These have found it to produce effective analgesia after meniscectomy, oral surgery, abdominal and orthopaedic surgery.[1–6] Ketorolac 10 mg was found to be as effective as morphine 10 mg.[7]

This present study set out to evaluate the efficacy and safety of ketorolac compared with morphine in the control of pain after laparotomy for gynaecological surgery. The primary assessment was the relative efficacy of the two treatments for pain control over the first 6 hours after the initial dose.

Method

Eighty women scheduled for laparotomy for gynaecological surgery were entered into the study which was approved by the local ethics committee; informed written consent was obtained from each patient. Exclusion criteria included peptic ulcer disease, severe systemic illness, asthma or other obstructive airways disease, addiction to alcohol or other drugs and allergy to morphine or aspirin-like drugs. Pregnant or lactating women were also not studied, nor patients taking long-acting analgesics or any other drugs likely to interfere with analgesic assessment.

A standard anaesthetic technique was used. Premedication was with papaveretum 20 mg and hyoscine 0.4 mg 60–90 minutes before surgery. Anaesthesia was induced with a sleep dose of thiopentone or propofol and maintained with nitrous oxide and halothane or isoflurane in oxygen. Muscle relaxation was provided with vecuronium that was reversed with neostigmine and atropine at the end of the procedure. The patients, after surgery, were randomly assigned to receive either ketorolac 30 mg intramuscularly (IM) as a loading dose and then 10 mg 4-hourly as required, or morphine 10 mg IM 4-hourly as required for postoperative analgesia in a double-blind fashion. The first dose of study medication was given when postoperative analgesia was requested by the patient.

Pain severity was assessed just before administration of analgesia using a 100-mm visual analogue scale with 'no pain' (0 mm) and 'worst pain imaginable' (100 mm) at the extremes, and on a four-point verbal scale of none (1), mild (2), moderate (3) or severe (4). These were repeated after 30 and 60 minutes and then hourly for 6 hours or until the second dose of study medication was required. Pain relief was assessed at the same times using a four-point verbal scale of none (1), slight (2), moderate (3) or complete (4). Arterial blood pressure, pulse and respiratory rates, and

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Table 1. Patient and surgery data.

	Ketorolac $n=40$	Morphine $n=40$
Age; years, mean (SD)	44.3 (9.7)	42.1 (8.9)
Weight; kg, mean (SD)	72.0 (10.4)	74.5 (14.2)
Duration of surgery; hours, median (range)	1.5 (1.0–2.5)	1.5 (1.0–4.5)
Type of surgery		
Hysterectomy	32	31
Ovarian surgery	4	2
Myomectomy	3	2
Colposuspension	0	1
Tubal surgery	1	2
Other	0	2

oxygen saturation, by pulse oximetry, were recorded at each instance. Any adverse effects were noted. The patients were asked for a global assessment of their pain and pain relief using the four-point verbal scales on the evening of day 1, and then at 24 and 48 hours, or until intramuscular analgesia was no longer required. The patient was withdrawn from the trial if pain relief was inadequate, and alternative medication given. A record was kept of all other medications administered during the study period.

Data were analysed statistically using the 2 sample *t*-test for parametric and the Wilcoxon Rank Sum test for nonparametric data. Pain intensity difference (PID) was calculated by subtracting the corresponding baseline value from the current pain intensity for each assessment. Summed pain intensity differences (SPID) were calculated by the trapezoidal rule as the areas under the PID-by-time curve.[8] Total pain relief (TOTPAR) was calculated according to the trapezoidal rule as the area under the pain-relief-by-time curve after adjustment for baseline pain. This was calculated over 4 hours and 6 hours after the first dose of study medication as a measure of the analgesic effectiveness of the drugs.

Missing pain and pain relief scores (due to patient sleeping) were estimated by linear interpolation of the recorded scores. A patient's last recorded score was assumed for subsequent scheduled assessments, if she withdrew for rescue analgesia.[9] Where a half-hour pain-relief score was missing, the median for that treatment was used as the estimated score.

Results

The groups were comparable with regard to age, weight, duration and type of surgery (Table 1). The detailed record cards for the first 6 hours of the study were lost for two of the patients and their results were therefore excluded from the summed pain intensity difference and total pain-relief score analyses. The record card data of pain and pain scores in the first 6 hours was totally inconsistent in one patient and was therefore removed from the analysis before the randomisation code was broken.

Table 2. Pain scores using the 4-point verbal scale.

Time (hours)	Ketorolac		Morphine	
	Median	Range	Median	Range
Baseline	4.0	3–4	4.0	2–4
0.5	3.0	2–4	3.0	2–4
1	3.0	2–4	3.0	2–4
2	3.0	2–4	3.0	1–4
3	3.0	1–4	2.0	1–4
4	3.0	1–4	3.0	1–4
5	3.0	1–4	3.0	1–4
6	3.0	1–4	3.0	2–4

Table 3. Pain relief scores.

Time (hours)	Ketorolac		Morphine	
	Median	Range	Median	Range
0.5	2.0	1–3	2.0	1–3
1	2.0	1–3	2.0	1–4
2	2.0	1–3	3.0	1–4
3	2.0	1–4	3.0	1–4
4	2.0	1–4	2.0	1–4
5	2.0	1–4	2.0	1–4
6	1.0	1–4	2.0	1–3

Baseline pain scores were similar in the two groups (Table 2, Fig. 1). The median time to the second dose of study medication was 4.67 hours (range 1.0–16.3 hours) in those who received ketorolac, which was not significantly different from the 4.63 hours (range 1.4–14.3 hours) in the morphine group. The pain and pain-relief scores in the first 6 hours are summarised in Tables 2 and 3, and Figure 1. The median pain score is similar in both groups using either the visual analogue or four-point verbal scoring system. The median summed pain intensity difference on the visual analogue scale was more negative with ketorolac than with morphine, implying more effective analgesia. However, the scores for morphine were better on the four-point verbal scale (Table 4). These differences did not reach statistical significance.

The range of summed pain intensity difference values for ketorolac on the visual analogue results includes some positive values, which reflected that in some cases the pain got worse after administration of analgesia. Pain-relief scores were better in the morphine group, although a statistically significant difference was not reached.

The patients' overall assessment of pain on the evening of day 1 and then at 24 hours were not significantly different between the groups ($p = 0.29/p = 0.28$). Pain relief scores were significantly better on day 1 ($p = 0.026$) in the morphine group but not at 24 hours ($p = 0.072$),

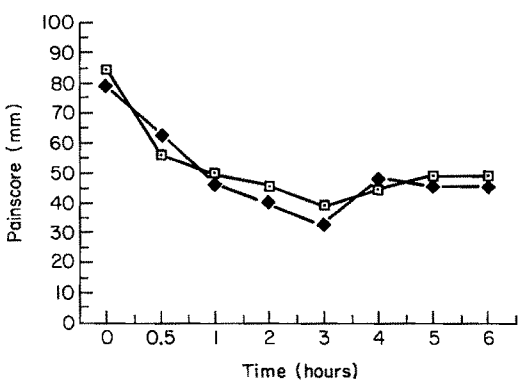

Fig. 1. Median pain scores in the first 6 hours after study analgesia using the visual analogue scale. ⊡, ketorolac; ◆, morphine.

Table 4. Summed pain intensity difference and total pain relief scores at 4 and 6 hours.

	Ketorolac			Morphine			
	Median	Minimum	Maximum	Median	Minimum	Maximum	P*
SPID using VAS pain scores							
4 hours	−117	−309	+18	−95	−268	−3	0.95
6 hours	−164	−483	+28	−138	−432	−11	0.57
SPID using 4-point verbal pain scores							
4 hours	−2.5	−9	0	−3.2	−8.5	0	0.091
6 hours	−3.5	−15	+0.5	−5.2	−14	+0.5	0.31
Total pain relief scores							
4 hours	7	3.5	12	8.4	4	12.5	0.061
6 hours	10	5.5	20	12.1	6	19.5	0.061

*Wilcoxon Rank Sum test.

(Figs 2 and 3). The overall observer assessment made as each patient completed the study favoured morphine over ketorolac ($p = 0.052$). (Table 5). There were no adverse effects on respiratory rate, arterial oxygen saturation or heart rate although one patient in the ketorolac group had unexplained hypotension (*vide infra*).

The reason for stopping study medication (Table 6) was mainly because the patient no longer required parenteral analgesia. Only two patients continued to receive study medication for 48 hours. Rescue analgesia was required in 13 patients in the ketorolac group and seven patients in the morphine group ($p = 0.19$, Pearson's Chi-square test). Study medication was stopped in one patient in each group due to adverse events: the patient in the ketorolac group became hypotensive and felt nauseated, shivery and unwell soon after the initial administration of the study drug. The patient in the morphine group developed a whole body macular rash. The most common unwanted effect in both groups, apart from the adverse events noted above, was nausea and vomiting; this affected 23 patients in the morphine group and 19 in the ketorolac group, but was not necessarily related to administration of the study medication since it quite often occurred before it was given. Three patients in the morphine group and one in the ketorolac group complained of feeling very sleepy.

Discussion

This study has demonstrated, in agreement with others, that ketorolac can provide acceptable analgesia in many patients with severe pain. Previous studies have compared various doses of ketorolac with each other and with morphine. Some have found ketorolac 30 mg and 90 mg similar or better than morphine 12 mg for patients with moderate or severe pain after major abdominal or orthopaedic surgery,[4,5] although others would disagree.[10] Ketorolac 30 mg and 90 mg has also been found to be better than pethidine 100 mg.[6,11] Oral ketorolac 10 mg in one study was

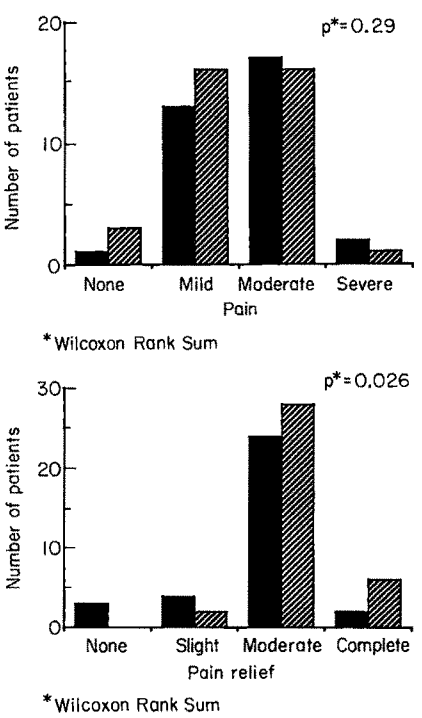

Fig. 2. Global assessment of pain and pain relief on day 1. ■, ketorolac; ▨, morphine.

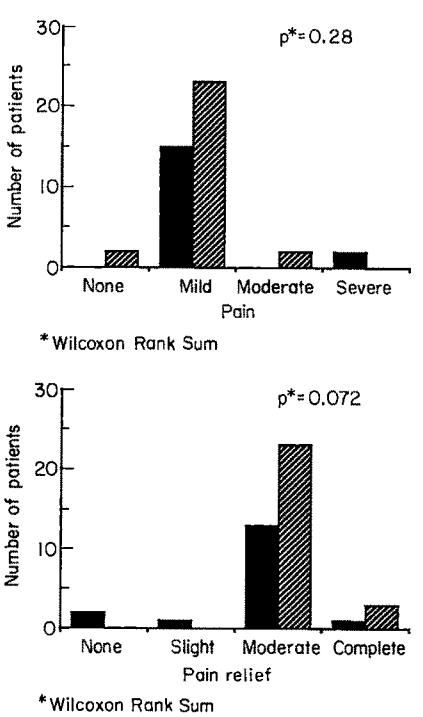

Fig. 3. Global assessment of pain and pain relief at 24 hours. ■, ketorolac; ▨, morphine.

Table 5. Observer's overall opinion.

	Ketorolac	Morphine
Very good	6	8
Good	13	18
Fair	7	10
Poor	14	4

p=0.052, Wilcoxon Rank Sum test.

Table 6. Reason for stopping.

	Ketorolac	Morphine
Completed 48 hours postoperatively	1	1
No longer required IM analgesia	25	31
Rescue analgesia given	13	7
Adverse events	1	1

as effective as morphine 10 mg intramuscularly for moderate/severe postoperative pain.[7] Studies also compared different doses of ketorolac. Some observed an increase in effectiveness with dose[4] whereas others found that the effective dose seems to plateau.[1,5,6] This may be related to the severity of the pain studied.

A loading dose of ketorolac 30 mg followed by maintenance doses of 10 mg were chosen in this study because there is evidence of gastric irritation when the dose exceeds 120 mg/day.[12] Clinically, ketorolac 30 mg provides more effective analgesia of longer duration than ketorolac 10 mg, with median time to remedication 6.0 hours after 30 mg compared with 4.9 hours with 10 mg. It was therefore decided that a loading dose of 30 mg would be given initially to establish reliably good pain relief, and then top-up doses of 10 mg to maintain analgesia, but with greater flexibility of dosing frequency and lower risk of gastric side effects.

Quality of postoperative pain relief is notoriously poor, and the fact that seven patients in the morphine group and 13 in the ketorolac required rescue analgesia demonstrates that both treatment regimens were inadequate for some patients in this study. Prescribers are reluctant to increase the dosage of opioid because of the risk of respiratory depression and excessive sedation. These two analgesic drugs interact with the pain pathways at different sites so their effects may be additive. It was shown that a background infusion of ketorolac 1.5 mg/hour reduced morphine requirements and significantly reduced pain scores in patients after upper abdominal surgery.[13] Addition of ketorolac to morphine analgesia should not increase the risk of respiratory depression since it does not have respiratory depressant effects.[13–15]

The different pain score result using the two different measurement systems probably reflects the fact that the results for the two drugs are very similar and a much larger study would be required to show whether or not a true difference exists. However, the marked difference in the scores for 'pain relief' are surprising. It would be expected that pain relief scores would correlate closely with pain scores. A possible source of error in this assessment in the first 6 hours of the study was that patients were asked how much pain relief they had had since their last assessment. Some patients interpreted this as overall pain relief since the injection, while others probably tended to take the question literally and compared pain with that at the previous assessment. If pain was mild at the previous assessment and still mild now, this might score 0 because there was no further pain relief, or 2 because the overall relief was good compared with the initial pain. This might explain the lack of correlation between pain score and pain-relief score in the first 6-hour assessments, but it does not explain the significant difference in overall assessment of pain relief on the evening of day 1. If the pain scores in the two groups are similar but the pain relief is considered to be better with morphine then perhaps this reflects higher cerebral effects of morphine affecting the patients' interpretation of their pain relief.

The high incidence of nausea and vomiting probably reflects the fact that this is a common symptom in this group of patients regardless of the type of postoperative analgesic used. Many of the patients were nauseated or vomiting before any study medication was given, and from this study it is not possible to discern whether there is any difference in the incidence of nausea and vomiting using ketorolac or morphine analgesia. The serious adverse event which occurred in one patient in the ketorolac group may have been related to the study drug. The hypotension was not associated with tachycardia and did not respond to fluid infusion. The vomiting persisted in spite of metoclopramide treatment and developed a 'coffee grounds' appearance after 10 hours. The patient was given two doses of ketorolac in total with an interval of 6 hours between them. She was withdrawn from the study after the appearance of 'coffee grounds' vomitus and given alternative analgesia for pain relief together with another dose of antiemetic and had no further problems. The whole episode may have been parasympathetically mediated and triggered by pain that was not well relieved in this patient. The appearance of altered blood in the vomitus may have been the result of gastric irritation by the ketorolac or possibly due to the trauma of recurrent vomiting. There are four previous reports of hypotension with ketorolac in a total of over 6000 administrations. All these cases occurred in the postoperative period and were believed to be because of surgical bleeding.

In conclusion, ketorolac provides acceptable analgesia in many patients with severe pain, but it has no apparent advantage over morphine in terms of pain relief or incidence of nausea and vomiting. It may have a place in the treatment of pain in patients in which the sedative effects of the opioids would be disadvantageous, e.g. patients with respiratory disease and those undergoing day-case surgery, or in combination with opioids to reduce opioid requirement and improve quality of analgesia.

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Clinical evaluation of double-burst stimulation

Its relationship to train-of-four stimulation

S. S. GILL, F. DONATI AND D. R. BEVAN

Summary

Double-burst stimulation was compared with train-of-four stimulation in 23 adult patients receiving atracurium. Train-of-four was interrupted in 11 subjects every 2 minutes by one double-burst stimulation, and re-applied 6–30 seconds later; the height of the first double-burst response, compared with its control, was depressed slightly more than T1. The relationship between double-burst stimulation ratio and train-of-four ratio was indistinguishable from the line of identity. The train-of-four response, if repeated more than 12 seconds after double-burst stimulation, was not depressed compared with pre double-burst stimulation values. Fifteen anaesthetists were asked to detect fade manually in the second part of the study, while train-of-four was recorded on the opposite arm. One hundred and fourteen determinations were made in 12 patients. Fade was detected manually more often with double-burst stimulation than with TOF.

Key words

Monitoring; neuromuscular function, train-of-four, double-burst stimulation.
Neuromuscular relaxants; atracurium.

Train-of-four (TOF) stimulation is used clinically to evaluate non-depolarising neuromuscular blockade.[1,2] However, one group of investigators reported that it is difficult to identify fade manually when T4/T1 (the ratio of the fourth twitch height to the first twitch height) has recovered to greater than 0.4.[3,4] Manual evaluation of TOF fade may be an insensitive test of residual neuromuscular blockade since clinical muscle weakness may be associated with a TOF ratio of 0.7 or less.[5–7] It has recently been suggested that double-burst stimulation (DBS) may be a more suitable pattern of nerve stimulation than TOF for identifying fade.[4,8–10] The DBS consists of two short tetanic stimulations that are seen or felt as two muscular contractions. Several stimulation patterns have been suggested, but the best results were obtained with two 50 Hz, 60-msecond trains separated by 750 mseconds.[10,11] The neuromuscular junction was found to take more than 3 seconds, but less than 15 seconds to return to the pre-DBS state. The above studies were conducted in patients receiving pancuronium, after suxamethonium had been used to facilitate tracheal intubation. The relationship between DBS and TOF has not been evaluated with the intermediate-acting non-depolarising neuromuscular blocking agents, without previous suxamethonium administration. The time interval required before a second application of DBS has not been determined in the range 3–15 seconds and only one group of investigators has reported that visual and tactile evaluation of TOF was unreliable,[3,4] and that DBS was superior during recovery from neuromuscular blockade.[4] This finding needs to be confirmed before DBS is applied widely.

This study was divided into two parts. The first involved stimulation of one arm with TOF interrupted by DBS during recovery from atracurium blockade. This was carried out to determine the relationship between the two forms of stimulation and the time required for the neuromuscular junction to return to its pre-DBS state. The second part of the study was a blinded evaluation of the ability of clinicians to detect TOF and DBS fade at various levels of neuromuscular recovery.

Methods

Twenty-three adult patients, ASA physical status 1 or 2, were studied during various elective surgical procedures of at least 60-minutes duration, after approval by the Hospital Ethics Committee. Patients with hepatic, renal, haematological, neuromuscular, metabolic, respiratory or cardiovascular disease or receiving medication known or suspected to affect neuromuscular transmission were excluded. There were 11 patients in part 1 and 12 in part 2 of the study.

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They were premedicated with diazepam 10 mg, orally, or pethidine 1 mg/kg with glycopyrronium 0.2 mg given intramuscularly one hour before surgery. ECG, arterial blood pressure and oxygen saturation were monitored on arrival in the operating room. Anaesthesia was induced with thiopentone 3–5 mg/kg and maintained with nitrous oxide 70% and isoflurane (up to 1% end-tidal) in oxygen.

Square pulses, 0.2 mseconds in duration, were applied supramaximally to the ulnar nerve at the elbow. TOF stimulation (2 Hz for 2 seconds) was applied every 12 seconds, but was interrupted for at least 12 seconds, when switching to DBS stimulation, and two 50-Hz, 60-msecond tetanic bursts were applied, separated by an interval of 750 mseconds.[4,11] Each burst consisted of three stimuli. The hand and forearm were immobilised in a splint and the force of contraction of the *adductor pollicis* muscle was measured with a force displacement transducer (Grass FT-10) and recorded on paper. Baselines for TOF and DBS were established after induction of anaesthesia while the lungs were ventilated manually with nitrous oxide, oxygen and isoflurane via a mask. Atracurium 0.5 mg/kg was then given intravenously as a single bolus. Tracheal intubation was accomplished when the twitch response was abolished. The lungs were ventilated using a system with a CO_2 absorber to maintain the measured end-tidal CO_2 partial pressure in the range 4.0–4.9 kPa. The CO_2 and isoflurane concentrations were measured by mass spectrometry. Increments of atracurium 0.1 mg/kg were given if required, after recovery from the initial bolus. Neuromuscular function was allowed to recover spontaneously as much as possible and data were collected during this phase. Appropriate doses of neostigmine and atropine were given at the end of surgery. No data were collected after administration of the anticholinesterase drug.

TOF was applied at 12-second intervals in the first part of the study, but this pattern was interrupted every 2 minutes to allow DBS stimulation. Application of DBS occurred after stopping TOF for at least 12 seconds. After DBS, the TOF was reapplied after 6, 12, 18, 24 or 30 seconds and at 12-second intervals thereafter; the first interval was selected at random, and changed after each DBS. The following variables were measured: the force of the control TOF and DBS responses; the time from injection of atracurium to return of the first twitch (T1) in the train-of-four, the first DBS response (DBS1), of the fourth twitch T4 of the train-of-four (T4), and of the second DBS response (DBS2); the height of DBS1, expressed as a percentage of DBS control, and T1 expressed as a percentage of T1 control, at 5% increments of T1; the DBS ratio (DBS2/DBS1) and the corresponding value of T4/T1 (TOF ratio), at 5% increments of TOF ratio; and the difference between T1 after DBS stimulation and T1 before DBS stimulation, expressed as a percentage of T1 control, for 6, 12, 18, 24 and 30 second delays.

The same anaesthetic and relaxant were given in the second part of the study. Train-of-four stimulation was applied to one arm every 12 seconds and the force of contraction of the *adductor pollicis* muscle was recorded. Fifteen anaesthetists, not involved with the case, who had no knowledge of the TOF ratio, were asked to detect fade by visual and tactile means using the opposite arm. For each determination, either TOF or DBS was applied first; the selection was made at random. The anaesthetist was asked whether or not he (she) could detect fade. The alternate mode of stimulation was then delivered, followed by the anaesthetists' response (fade or no fade). These assessments were made when the measured T4/T1 was in the range of 10–90%. Results are presented as mean (SEM) unless otherwise specified. Paired Student's *t*-test was applied when appropriate. The number of assessors who detected fade for part 2 of the study was evaluated for each 10% range of TOF ratio, from 10 to 90%. A Chi-squared test was used for each range to detect differences between DBS and TOF. Differences were considered statistically significant when $p < 0.05$.

Results

There were eight females and three males in part 1 and their mean age (SD) was 55.6 (12.6) years and mean weight 60.6

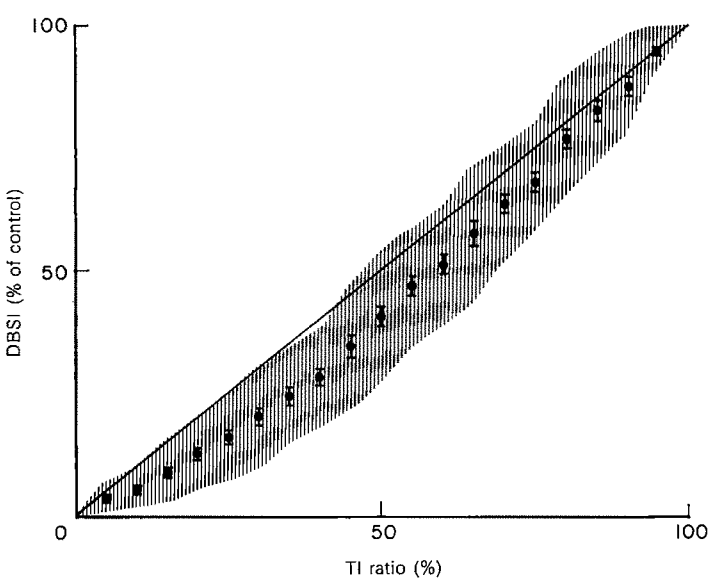

Fig. 1. The relationship between DBS1 (first response to DBS) to T1 (the first response to TOF stimulation) as a percentage of control (SEM). The shaded zone shows the 95% confidence limits. The thin line shows the line of identity.

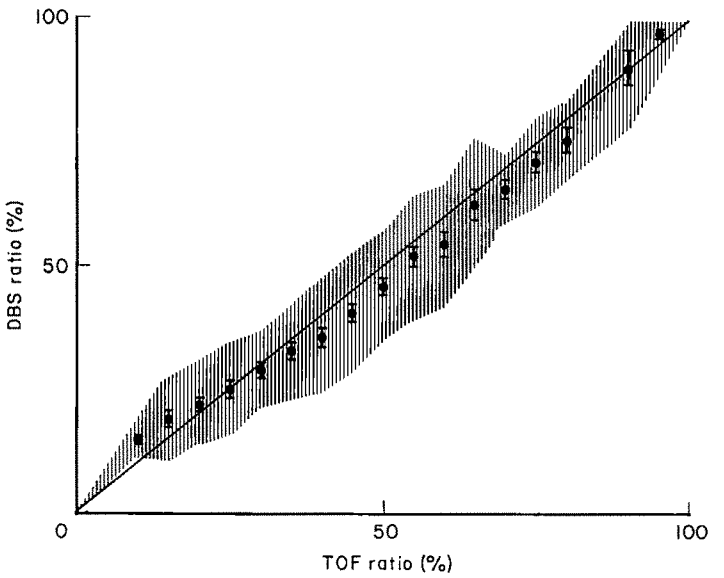

Fig. 2. The relationship between DBS ratio (the height of the second to that of the first twitch during DBS) and the TOF ratio (the amplitude of the fourth to the amplitude of the first twitch during TOF stimulation) as a percentage (SEM). The shaded zone shows the 95% confidence limits. The thin line shows the line of identity.

(10.8) kg. There were nine females and three males in part 2 and their mean age was 49.5 (13.9) years and mean weight 65.4 (12.7) kg. The control height of DBS was 2.70 (SEM) 0.14 times that of TOF. The response to DBS reappeared a short time before TOF. Time from injection of atracurium to reappearance of the first response to TOF stimulation (T1) was 38.4 (1.7) minutes and for DBS (DBS1) 36.2 (2.1) minutes ($p = 0.01$). Time to the first T4 response was 51.2 (2.0) minutes compared with 48.6 (2.3) minutes for the second DBS response (DBS2) ($p < 0.01$). The height of DBS1 relative to control was depressed to a slightly greater extent than T1/control (Fig. 1). The relationship of the DBS ratio (DBS2/DBS1) and the TOF ratio is shown in Fig. 2. It did not deviate significantly from the line of identity. DBS ratio was 65.8 (1.8) when T4/T1 was 70%.

Double-burst stimulation affected the height of subsequent T1 (Fig. 3). If TOF stimulation was applied 6 seconds after DBS, T1 was 1.8 (0.3%) (relative to control) lower than the T1 response immediately preceding DBS. If an interval of 12 seconds was allowed after DBS, T1 was 1.6 (0.1%) greater than before DBS ($p = 0.0001$ compared with 6 seconds). There were no changes in T1 heights in the range of intervals between 12 and 30 seconds.

One hundred and fourteen paired determinations were made in part 2 of the study. Fade was detected only 26 times (23%) with TOF, but with DBS, the detection rate increased to 77/114 (68%) ($p < 0.0001$). Ninety-one determinations were made for TOF ratio < 70%. Fade was detected in 26 instances with TOF (29%), compared with 81 instances with DBS (89%). DBS fade was most often

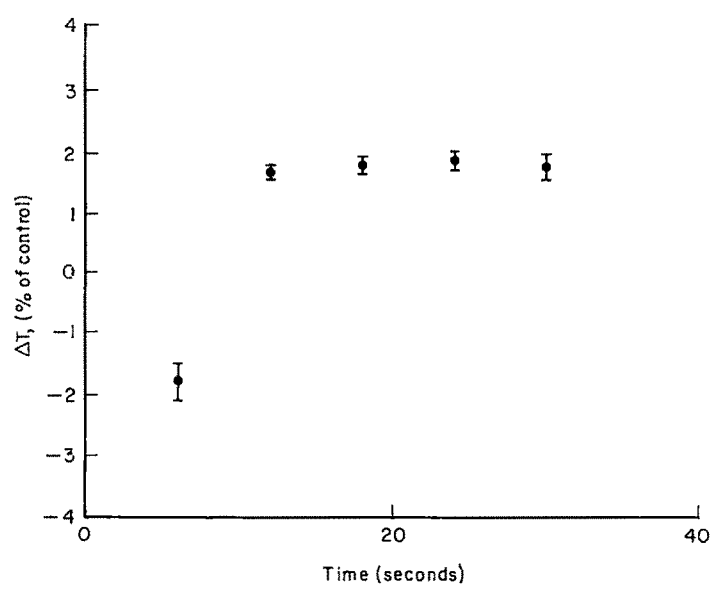

Fig. 3. The change in the height of T1 (as 0% of prerelaxant control) after DBS compared with the pre-DBS value, versus the time interval between DBS and the next TOF.

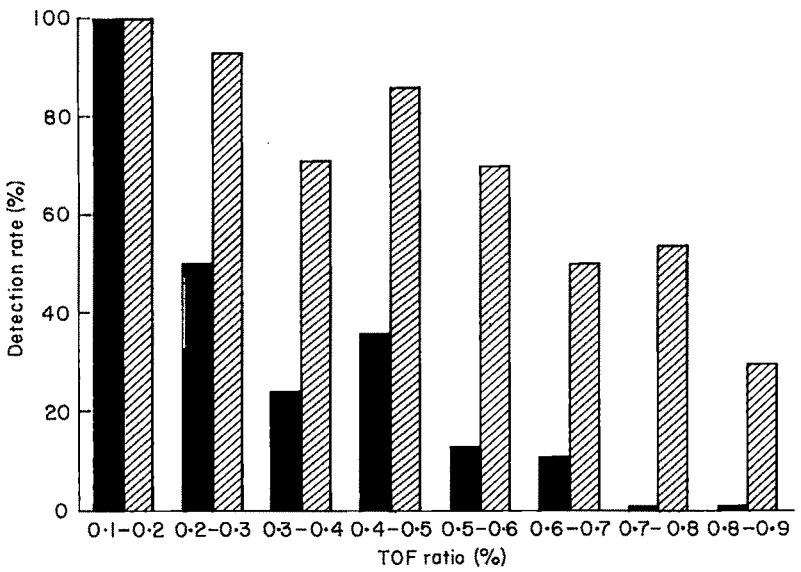

Fig. 4. Visual and tactile detection rate of fade for DBS (▨) and TOF (■) at various levels of TOF ratio.

detected (23/26 times: 88%) when fade was detected with TOF (26 times). However, detection of DBS fade was infrequently associated with simultaneous TOF fade detection (23/77: 30%).

Detection rate for both modes of stimulation increased as fade increased (Table 1, Fig. 4). However, for each range of values, DBS stimulation was associated with a greater detection rate.

Discussion

This study showed that DBS exhibits the following characteristics when used during spontaneous recovery from atracurium blockade: depression of first DBS response (DBS1) usually exceeds that of T1; the DBS ratio (DBS2/DBS1) is numerically close to the TOF ratio (T4/T1); at least 12 seconds must elapse after DBS for the neuromuscular junction to return to its pre-DBS state, and the force of contraction of the response to DBS is greater than after TOF stimulation. It was also demonstrated that manual detection of TOF fade cannot reliably be accomplished even at T4/T1 less than 30%. However, the presence of fade, or residual blockade, was identified more often with DBS. The response to DBS could be first detected 2.2 minutes before the first response T1, but this difference, although statistically significant, is of no clinical importance. Similarly, the reappearance of DBS2, which occurred 2.6 minutes earlier than T4, was statistically significant, but clinically unimportant. An earlier return of DBS compared with TOF responses was also reported by Neilson *et al.*, who showed that the first response to DBS after atracurium corresponded to a post-tetanic count (PTC) of four.[8] The same group showed that with atracurium, a PTC of 4 preceded detectable T1 by no more than 4 minutes.[12] However, these authors applied TOF stimulation every 10 seconds. It is possible that the interval between TOF in their study (8 seconds) might have depressed TOF response slightly more than in the current study, where 10-second intervals were used. This may explain why the difference observed between the reappearance of DBS1 and T1 was slightly less in the current study (2.2 minutes). Clinically, it does not appear that DBS can detect intense blockade not detectable by TOF stimulation. Thus, DBS is not a substitute for PTC[12,13] in the monitoring of intense blockade.

Table 1.

Measured TOF	Detection rate with TOF		Detection rate with DBS		p
0.11–0.20	5/5	100%	5/5	100%	N.S.
0.21–0.30	7/14	50%	13/14	93%	0.02
0.31–0.40	4/17	24%	12/17	71%	0.01
0.41–0.50	5/14	36%	12/14	86%	0.01
0.51–0.60	3/23	13%	16/23	70%	0.001
0.61–0.70	2/18	11%	9/18	50%	0.02
0.71–0.80	0/13	0%	7/13	54%	0.005
0.81–0.90	0/10	0%	3/10	30%	N.S.

N.S. not significant.

DBS1 was depressed slightly more than T1, when compared with their respective controls. This is probably because DBS1 is the superimposition of three contractions. The last two of these contractions are likely to be depressed more than the first, with non-depolarising blockade, i.e. some degree of tetanic fade exists. Thus, the sum of the three contractions is depressed to a greater extent than the first twitch of TOF. The DBS and TOF ratios were depressed to a similar extent. Engbaek *et al.*[11] reported a similar finding in the presence of blockade produced by pancuronium after suxamethonium, instead of atracurium as in this study. The DBS ratio can be decreased if the second burst is made up of fewer contractions than the first.[8] However, this pattern may lead to the detection of fade in the absence of neuromuscular blockade.[11] Thus, the use of two bursts with an equal number of stimuli is preferred.

The present study also suggests that DBS may be repeated at intervals of no less than 12 seconds, which indicates that DBS stresses the neuromuscular apparatus to a similar extent as TOF stimulation.[14] There was a slight

increase in the height of T1 compared with pre-DBS T1 if TOF stimulation was applied after 12–30 seconds after DBS. This may be the reflection of a slight facilitation or spontaneous recovery of the relaxant. However, this increase is of no clinical importance since T1 remains within 2% of its previous height. The depression of T1 after 6 seconds post-DBS is probably the result of transmitter depletion and it is therefore recommended not to repeat the DBS within 12 seconds. This interval is somewhat shorter than suggested in another study,[11] in which 15 seconds appeared adequate.

The fade observed with double-burst stimulation, which consists of two short tetani (50 Hz for 60 mseconds) separated by 750 mseconds is numerically close to that obtained with TOF. Thus, one cannot attribute the differences in manual detection rates associated with the two forms of stimulation to different degrees of fade. Instead, the characteristics of the human senses probably account for the differences. One factor is probably that the strength of the contractions are, with DBS, almost three times as large, which makes them easier to feel. Also, DBS is seen and felt as two contractions, which are probably easier to compare than two contractions (the first and the fourth) separated by two others (the second and the third). In any event, understanding which mechanisms are important in the visual and tactile evaluation of muscular contractions would be helpful. The yield of DBS could be improved by changing the duration of each burst; the interval; or the stimulation frequency. The number of permutations is very large, and ideally, each requires a blinded clinical study for assessment. It would be impractical to carry out such a study unless the important characteristics of human senses were known to focus the search. Nevertheless, a limited number of patterns have been tried.[11] The pattern which was chosen appears at least as good as the others and represents a significant improvement over TOF stimulation.

The anaesthetists who assessed blockade used neuromuscular monitoring routinely in their practice and were aware of their limited ability to detect TOF fade by tactile and visual evaluation.[3] Their performance was still poorer (36%) than the 'moderately experienced observers' (56%) in Viby-Mogensen's initial study[3] in detecting TOF ratios in the range 0.41–0.50% but seemingly better than the observers used in the same group's more recent study (about 20%).[4] Part of the discrepancy might be because of differences between the two arms,[15] and these differences might be greater if a shorter acting relaxant (atracurium in this study as opposed to pancuronium) is used. Nevertheless, it appears that manual detection of TOF fade is difficult and awareness of this difficulty does not improve detection rate, despite careful assessment. However, detection of DBS was much greater, even if none of the assessors had used this mode of stimulation previously.

It appears that more DBS fade was detected in the present study for TOF ratio > 70% (30–54%) than reported in Drenck *et al.*'s article (about 15%). The discrepancy may be the result of the different relaxant used, the different distribution of TOF values in the range 0.71–1.00, and differences between arms. The presence of a possibly high 'false positive' rate is not a drawback of the method, and may even be an advantage. Many patients demonstrate clinical signs of weakness, in spite of TOF ratio > 0.7.[16] It is probably better to err on the side of caution. The use of TOF monitoring with tactile or visual evaluation might explain the unacceptably high incidence of postoperative residual weakness reported, in spite of the use of nerve stimulators.[16] The use of DBS might improve the detection of weakness, but two factors need to be considered. First even if DBS is a more sensitive test than TOF in the detection of fade, 11% of patients with residual neuromuscular blockade, defined as TOF ratio < 70%, remained undetected with DBS. Second, the mere presence of a monitoring modality does not guarantee the avoidance of complications. In other words, DBS needs to be used at the appropriate time, and detection of residual blockade should be followed by appropriate management. It is recommended because of the better performance of DBS when compared with TOF in the assessment of residual neuromuscular blockade, that this new modality be available on commercial nerve stimulators.

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Impairment of left ventricular diastolic function during coronary artery bypass grafting

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Summary

Twelve patients were studied by transoesophageal Doppler echocardiography to determine diastolic function during coronary artery bypass grafting. Haemodynamic and Doppler-derived variables were measured after induction of anaesthesia and after closure of the sternum. Early diastolic filling of the left ventricle decreased from 55% to 35% during surgery. The contribution of atrial contraction to left ventricular filling increased from 41% to 62% ($p < 0.001$). We conclude that coronary artery bypass grafting results in impairment of diastolic function during the operation.

Key words

Heart; myocardial function.
Measurement techniques; echocardiography, transoesophageal Doppler.

Coronary artery bypass grafting (CABG) may be associated with the development of a low cardiac output state without evidence of intra-operative myocardial ischaemia. Some of these patients show a poor response to stimulation with positive inotropic agents. They are usually noted to have a normal left ventricular (LV) systolic function before surgery. Using transoesophageal echocardiography, we have observed patients with a low cardiac output but evidence of normal LV systolic function. Thus, the aim of our study was to determine whether diastolic function is altered predictably in the early phase after extracorporeal circulation.

Methods

Twelve consecutive patients (mean age 55.7 years) scheduled for coronary revascularisation gave their informed consent to this institutionally approved study. All patients had a normal pre-operative left ventricular systolic function with an ejection fraction > 65%. Eight patients had a history of arterial hypertension which was controlled effectively with antihypertensive medication. The patients were premedicated with midazolam 0.1 mg/kg intramuscularly. In the operating room, electrocardiogram (ECG) leads were connected and an intra-arterial catheter was inserted into the left radial artery. Anaesthesia was induced with fentanyl, flunitrazepam and etomidate, and pancuronium administered. The trachea was intubated and controlled mechanical ventilation was instituted with an F_{IO_2} of 0.5 (F_{IN_2} 0.5). Maintenance of anaesthesia was accomplished with intravenous supplementation of fentanyl and flunitrazepam. A 7.5-FG flow-directed thermodilution Paceport catheter (American Edwards, Irvine, California, USA) was then inserted via the right internal jugular vein to measure haemodynamic parameters. A Toshiba 5 MHz transoesophageal Doppler probe was introduced with the aid of a laryngoscope. The transducer was positioned behind the left atrium and angled down towards the apex by retroflexion, and obtained a four-chamber view of the heart. This position of the transducer allows easy examination of blood flow through the mitral valve. The sample volume was placed between the mitral annulus and leaflet tips to make the ultrasound beam as parallel to flow as possible. All echocardiographic data were recorded continuously on videocassettes. Assessment of the videotapes was performed by an independent cardiologist (K.R.).

Haemodynamic data (mean arterial pressure, heart rate, central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, cardiac output, and stroke volume) were recorded before surgical incision and after closure of the sternum. Doppler measurements were performed at the same two stages, i.e. before and at the end of operation. Measurements from three consecutive cardiac cycles were averaged at each examination. The diastolic filling period was defined as the interval from the upstroke to the downstroke of the Doppler signal. Early peak diastolic velocity (E) and peak atrial velocity (A) were measured as shown in Figure 1. The total area under the

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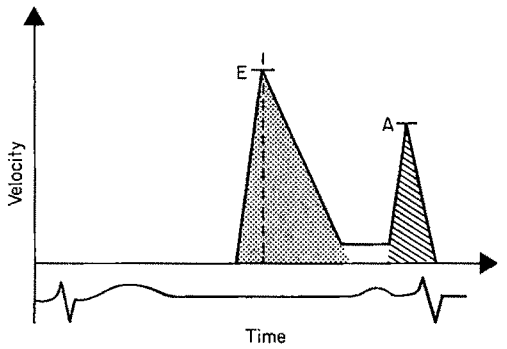

Fig. 1. Schematic drawing of mitral flow velocity: E represents peak diastolic velocity and A peak atrial velocity.

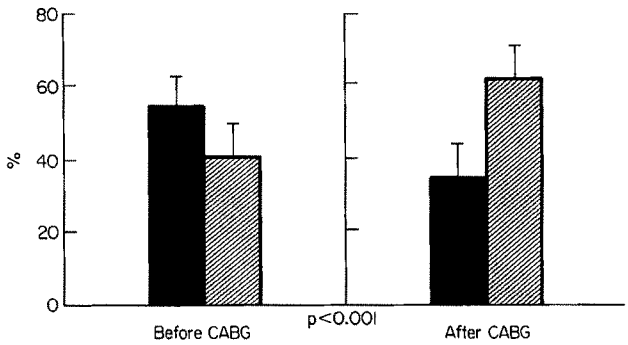

Fig. 2. Participation (in %) of early diastolic filling and atrial contraction in left ventricular filling during coronary artery bypass grafting (CABG). Results are given as mean and standard deviation. ■, early diastolic filling; ▨, atrial contraction.

velocity curve represents the entire diastolic filling period; the initial phase characterised early diastolic filling (EDF) and the second phase atrial contraction (AC).

Haemodynamic and Doppler measurements from each examination were compared using the paired *t*-test or Wilcoxon test as applicable.

Results

A selection of haemodynamic data before and at the end of operation is given in Table 1. Cardiac output after CABG was not different from the initial value. Stroke volume was reduced because of a significant increase in heart rate. There were no significant differences between the temperatures (nasopharyngeal, pulmonary arterial, rectal) measured before and after CABG.

Measured flow velocities showed significant differences between the two examination phases. Early peak diastolic velocity (E) was reduced after CABG with a simultaneous increase in peak atrial velocity (Table 2). Determination of the time velocity integral (the area under the velocity curve) revealed that early diastolic filling (EDF) of the left ventricle decreased significantly from 55% before to 35% after CABG (Fig. 2). In contrast, the contribution of atrial contraction to LV filling increased significantly from 41% to 62% at the end of operation.

Discussion

Transoesophageal echocardiography was introduced initially by Frazin *et al.*[1] Its validity and usefulness in monitoring changes in ventricular function during cardiac surgery were confirmed.[2] Diastolic abnormalities of LV function are recognised in patients with hypertrophic cardiomyopathy, amyloid heart disease, and coronary artery disease.[3-5] Doppler echocardiography was compared with angiographic techniques, and was found to be a reliable, noninvasive tool for assessment of diastolic performance.[6,7] The mitral flow velocities as measured by the Doppler method are influenced directly by alterations in LV filling, thus allowing easy beat-to-beat recognition of changes in diastolic LV function.[8]

We used transoesophageal Doppler echocardiography in our study to evaluate diastolic function before and after CABG. Early diastolic filling decreased, and the contribution of atrial contraction to LV filling increased during the operation, which indicated intra-operative impairment of diastolic function. Myocardial ischaemia on the evidence of ECG (lead V_5) or enzyme studies did not occur in any of our patients. Alterations in preload may mimic or mask diastolic dysfunction.[9] In this study, the preload of the left ventricle was kept constant at both measurement phases. Nitroglycerine was not administered. The influence of heart rate changes on diastolic filling was examined by Oka *et al.*,[10] who found only minor effects. Our results, which suggest the intra-operative development of diastolic dysfunction are supported by the findings of Rinder *et al.*,[11] who reported that the indices of diastolic filling returned to baseline within 18 hours after coronary revascularisation.

Atrial contraction assumes a greater part in ventricular filling when early diastolic filling is reduced. This means that atrial contraction becomes more important,[12] which underlines the relevance of a normal sinus rhythm in the early period after bypass.

The clinical significance of left ventricular diastolic function has been recognised only recently.[8] Diastolic function is determined partially by intrinsic properties such as myocardial stiffness, relaxation rate, and passive chamber stiffness. Diastolic impairment with subsequent cardiovas-

Table 1. Haemodynamic variables before and after coronary artery bypass grafting (CABG).

	Before CABG	After CABG
MAP (mmHg)	89 (10)	84 (11)
HR (beats/minute)	66 (9)	97 (13)***
PAP systolic (mmHg)	26 (8)	28 (5)
PAP diastolic (mmHg)	11 (5)	12 (4)
PCWP (mmHg)	9 (5)	9 (5)
SV (ml)	68 (9)	57 (8)***

MAP, mean systemic arterial pressure; HR, heart rate; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; SV, stroke volume. Results are given as mean (SD). ***$p < 0.001$.

Table 2. Measured early peak diastolic velocity (V_{max}EDF) and peak atrial velocity (V_{max}AC). Values are mean (SD).

	Before CABG	After CABG
V_{max}EDF (cm/second)	30 (9)	24 (9)***
V_{max}AC (cm/second)	40 (6)	46 (10)***

***$p < 0.001$.

cular depression may not respond to positive inotropic drugs. In contrast, agents with known negative inotropic properties, in particular calcium-channel blockers such as diltiazem, may be advantageous in patients with diastolic dysfunction.

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CASE REPORT

Opisthotonus and other unusual neurological sequelae after outpatient anaesthesia

P. R. I. SAUNDERS AND M. N. E. HARRIS

Summary

Four patients who developed unusual neurological sequelae after outpatient anaesthesia are described. Propofol is strongly implicated as the cause. All four patients were female with no previous history of psychiatric disorder or neurological disease, unpremedicated, and had procedures of duration less than 20 minutes. Hyperreflexia and hypertonicity were present postoperatively and the reactions appeared to be triggered by an external stimulus. Three patients were examined by a neurologist and had a normal electroencephalograph. Two patients were on the same operating list; quality control was carried out on the anaesthetic agents used, and blood samples sent for toxicology showed no abnormalities. Mechanisms underlying these reactions are discussed.

Key words

Anaesthetics; intravenous, propofol.
Complications; neurological, hyperreflexia, opisthotonus.

Outpatient surgery for short operations continues to gain momentum and propofol meets many of the requirements for an induction agent for such procedures. It is short-acting, noncumulative, provides good quality of anaesthesia, and in unpremedicated patients there is a rapid recovery with clearheadedness.[1–4] The Committee on Safety of Medicines (CSM) drew attention in August 1987 to nine reports of 'convulsions' and involuntary movements which occurred during induction or emergence from anaesthesia induced by propofol.[5] The CSM drew attention in May 1989 to a total of 37 reports of 'seizures' and 16 reports of involuntary movements associated with the use of propofol. In addition, opisthotonus had occurred in 10 patients. They advised that care should be taken when this drug was used to anaesthetise epileptic patients.[6] Four of the reports of cases that involved opisthotonus were published recently.[7–10] In man, opisthotonus is the most severe motor manifestation seen in decerebration after brain injury.[11] There were no previous reports in man linking opisthotonus with clinically used anaesthetic agents before the introduction of propofol. Hyperreflexia is a well documented and common neurological sequela after general anaesthesia and, although self-limiting in these circumstances, is likened to decerebrate rigidity.[12–14] Opisthotonus is a broadly facilitated state of muscle stretch reflexes. Previously published reports have failed to emphasise a possible common physiological basis which may explain a wide range of unusual neurological sequelae of varying duration and intensity after outpatient anaesthesia.[7–10,15,16]

Case histories

Case 1

A 44-year-old moderately anxious female patient (weight 50 kg) with a 6-month history of haematuria presented for outpatient dilatation and curettage, and cystoscopy. She had previously had numerous inpatient general anaesthetics with a thiopentone and halothane technique with no adverse effects and had no history of psychiatric disorder, epilepsy or other neurological disease. She was unpremedicated. She received atropine 0.3 mg and alfentanil 0.5 mg followed by 12 ml of a solution that contained propofol 9.5 mg/ml with lignocaine 0.5 mg/ml. Induction was smooth, and anaesthesia was maintained with enflurane 1.5% and nitrous oxide 65% in oxygen at a flow rate of 9 litres/

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minute via a Bain system; the patient breathed spontaneously. The operating time was 20 minutes. She was unresponsive to painful stimulus or verbal command in the recovery area 15 minutes after the end of the operation. Rapid rhythmical jerky movements of eyes and eyelids were noted. Her pupils were normal. She had hypertonicity and hyperreflexia, more pronounced in the lower limbs and on the left side, and ankle clonus was present. The plantar reflexes were downward. There were no cardiorespiratory problems. Blood sugar was normal. She was still unresponsive when examined by a neurologist 2 hours after operation. Hyperreflexia and hypertonicity persisted but now were elicited only in the lower limbs, with absent ankle clonus and downgoing plantars. The rapid rhythmical jerky movements of the eyelids remained but the jerky movements of the eyes were now irregular and of varying intensity. The eye movements were conjugate and there was no phasic or pendular nystagmus. Corneal reflexes were brisk. No neck stiffness was elicited. A sudden tonic spasm lasting 2 seconds, with arching of the back and neck extension, occurred near the end of her neurological examination whilst the vestibulo-ocular reflexes were being tested. The recovery nurse then described a similar episode which had occurred earlier, whilst she was measuring the blood pressure. Two further random episodes of similar brevity and nature occurred. The limbs and face did not move during these episodes. An electroencephalograph (EEG) at this time showed no epileptiform activity. Four hours after operation she was grimacing in response to painful stimulus, and showed a weak but unreliable response to verbal command. There was now a time of fluctuating consciousness. She regained consciousness one hour later but was still drowsy. Her conscious level continued to improve, but she had decreased muscle power in her hands and feet and hyperreflexia and hypertonicity persisted, although to a lesser extent. These signs had localised to the right side 10 hours after the operation and in addition she complained of neck stiffness. Pupils were normal, there was no evidence of papilloedema and she had a negative Kernig's sign. Computerised tomography at this time showed no evidence of a subarachnoid haemorrhage. A lumbar puncture was performed; biochemistry and microscopy of cerebrospinal fluid were normal. She developed rapid rhythmical jerky movements of the eyelids 24 hours later, while neck flexion was being tested. She was unresponsive to verbal command and painful stimulus, and hyperreflexia persisted. This episode lasted 15 minutes and she was then responsive but drowsy. She remained generally weak for the next 3 days. She was discharged 6 days after operation with no abnormal residual neurological features. All investigations, including full blood count, biochemical screen, thyroid function tests and urine and blood for toxicology were normal.

Case 2

A 24-year-old moderately anxious female patient (weight 45 kg) with a 6-month history of abdominal pain presented for outpatient diagnostic laparoscopy. She had no previous anaesthetic history and had no history of psychiatric disorder, epilepsy or other neurological disease. She was unpremedicated. She received atropine 0.3 mg and alfentanil 0.5 mg, followed by 12 ml of propofol 9.5 mg/ml with lignocaine 0.5 mg/ml. Induction was smooth. Vecuronium 5 mg was given and anaesthesia was maintained with enflurane (0.8%). The lungs were ventilated artificially with a Nuffield Penlon 200 series ventilator attached to a Bain system with nitrous oxide 65% in oxygen at a flow rate of 6 litres/minute. Operating time was 15 minutes. She was given glycopyrronium 0.5 mg and neostigmine 2.5 mg at the end of the procedure and developed generalised coarse asynchronous jerky movements similar to those seen with residual neuromuscular blockade. The nerve stimulator confirmed adequate reversal but on clinical grounds administration of glycopyrronium 0.5 mg and neostigmine 2.5 mg was repeated. She failed to respond to verbal command or painful stimulus for one hour. Blood sugar was normal. Hypertonicity and hyperreflexia were elicited in all limbs, particularly the lower limbs, and ankle clonus and rapid fine rhythmical jerky movements of the eyelids and eyes were observed. These subsided when she regained consciousness but less pronounced hyperreflexia remained. She was examined by a neurologist 4 hours after operation. He found no signs of any neurological deficit and she had obviously made a complete recovery. EEG performed at that time showed no epileptiform activity. She remained tired for the next 24 hours. She stated that she had been aware of being in recovery in those early stages. She could see blurred faces and hear voices which appeared distant but understandable. She wished to, but was unable, to respond to their verbal commands, e.g. 'squeeze my finger'. She felt the pinprick when her blood sugar was estimated but was unable to withdraw her finger or state that it was painful. Biochemical screen, thyroid function tests and urine and blood for toxicology were normal.

Case 3

A 21-year-old female patient (weight 70 kg) presented for outpatient laparoscopy for investigation of infertility. She had never had general anaesthesia before, and had no history of psychiatric disorder, epilepsy or other neurological diseases. She was unpremedicated. She received atropine 0.3 mg and alfentanil 0.5 mg/ml, followed by 14 ml of propofol 9.5 mg/ml with lignocaine 0.5 mg/ml. Induction was smooth. Atracurium 25 mg was given and anaesthesia was maintained with enflurane (1%). The lungs were ventilated artificially with a Nuffield Penlon 200 series ventilator attached to a Bain system with nitrous oxide 65% in oxygen at a flow rate of 9 litres/minute. Operating time was 10 minutes. Residual neuromuscular blockade was reversed with glycopyrronium 0.5 mg and neostigmine 2.5 mg. She was fully conscious 5 minutes after her arrival in the recovery area and then developed a series of well defined extensor jerks of all four limbs over 15 seconds; her eyes were shut at this time as if still asleep. She developed fine 'shivering' in all four limbs one minute later, but was able to open her eyes and speak appropriately. She had a further similar episode shortly afterwards but was responding appropriately to questions within seconds. The first episode was associated with the recovery nurse taking the blood pressure. There was hyperreflexia and hypertonicity in the lower limbs without ankle clonus and the plantars were downgoing. She was examined by a neurologist one hour after operation; hyperreflexia was noted. She had an episode of 'absence' during the examination when the eyes were open but there was impaired accessibility. Some preservation of movement was demonstrated, but she did

not respond to repeated verbal instructions to touch her nose. She had another episode of three brief 'shock-like' jerks, which were tonic spasms, 5 seconds later. The lower limbs were already in the extended position and the upper limbs in the mid-flexed position. An EEG was performed and the patient fluctuated between alertness and drowsiness during the procedure but no epileptiform activity could be demonstrated. She was discharged 3 hours later; she was alert and there had been no further intervening unusual neurological sequelae. All investigations including full blood count, biochemical screen, thyroid function tests and urine and blood for toxicology, were normal.

Case 4

A 26-year-old extremely anxious female patient (weight 50 kg) with a recurrent history of ear infections presented for outpatient bilateral myringotomies. She had no history of psychiatric disorder, epilepsy or other neurological disease. She was unpremedicated. Anaesthesia was induced with propofol 150 mg and maintained with isoflurane (2%) with nitrous oxide 65% in oxygen at a flow rate of 9 litres/minute via a Bain system, breathing spontaneously. The operating time was 10 minutes. She started to gasp for breath and became restless as the recovery room nurse was measuring the blood pressure. An anaesthetist who was summoned found that she was not breathing. There was generalised increased tone and her back was arched, the neck was fully extended and jaws were clenched. Her legs were fully extended and the elbows were extended with flexion and pronation of the wrists. Her mouth could not be opened to introduce an oropharyngeal airway, and manual ventilation was impossible. This lasted 15 to 30 seconds and then subsided. She had two further similar episodes but she remained acyanotic throughout. She regained consciousness 3 minutes after the last episode and her breathing pattern was normal. She was discharged 4 hours later without any investigation.

Discussion

The CSM drew attention in May 1989 to 37 reports of 'seizures' (13 of these reports concerned known epileptics). A seizure is considered epileptic in nature unless stated otherwise and this implies cortical disturbance detected as EEG changes.[17] Propofol causes marked cortical depression with an isoelectric EEG. It has been used successfully to treat status epilepticus and is known to reduce seizure length in patients undergoing ECT.[18–21] This suggests that propofol is not an epileptogenic drug. However, drug-induced decerebrate rigidity, a self-limiting condition, can account for opisthotonic and myoclonic manifestations in association with a normal EEG.

There has been considerable confusion over the years in the literature about accurate definition of the neurophysiological basis for the variety of excitatory responses seen in patients during induction and recovery from general anaesthesia. It is known that central nervous system excitation occurs during induction of anaesthesia. Guedel in 1933 developed his classic table of the signs of anaesthesia with division into stages and planes using open ether. The second stage was classified as excitement or uninhibited response and it represented a period of muscular activity associated with increased muscle tone.[22] This can be minimised by adequate premedication, psychological reassurance, quiet surroundings and rapid smooth induction. It tends to occur in young, muscular, nervous individuals who have had relatively short procedures.

Postanaesthetic shivering has frequently been confused with thermoregulatory shivering. The former is tonic rigidity with generalised coarse phasic tremor. Core temperature is frequently normal and piloerection, a characteristic feature of thermoregulatory shivering, is absent. Johnson likened postoperative rigidity to decerebrate rigidity, with clonus and exaggerated tendon reflexes.[14] Again, it tends to occur in young, muscular individuals who have had relatively short procedures.

Soliman and Gillies drew attention to the appearance of muscle spasticity in nearly all postoperative patients.[12] They noted that the spasticity occurred when the patient started to respond to a painful stimulus and disappeared when the patient was responding to verbal commands. They noted that the reticular formation gains its activity before the higher centres, where depression of the supraspinal inhibitory pathways results in a period of facilitation in the anterior horn cells. Postanaesthetic shivering and thermoregulatory shivering, even though they have different clinical manifestations, both result from a critical level of facilitation being reached in the anterior horn cells.

The classic decerebrate model described by Sherrington involves rigidity of the extensor muscles that follows midcollicular separation of the midbrain from the spinal cord and it is supported by an overactive stretch reflex as a result of facilitation of γ-efferent neurones.[11,23] Clinically, decerebration is perhaps considered best as a heterogeneous spectrum of motor manifestations resulting from brain injury. Opisthotonus may result and there may be unilateral or alternating motor activities. It may be accompanied by preservation of consciousness.[11]

Bremer noted that section of the brainstem at midcollicular level causes the EEG to become slow, synchronised and sleep-like. Consequently, it is probable that midcollicular decerebration deprives the midbrain of inhibitory influences from the cortex that normally restrain it, and deprives the cortex of excitatory influences that normally facilitate it; thus the midbrain and spinal cord overreact while the cortex 'sleeps'.[23]

The midbrain reticular formation is considered to be one of the most important sites for the regulation of wakefulness, natural sleep and anaesthetic state. Each neurone in this area shows the characteristic features of excitatory as well as inhibitory responses by various stimuli. All anaesthetic agents, except nitrous oxide, have depressant effects on the excitatory responses evoked by somatosensory stimuli and this is probably the fundamental basis of the anaesthetic state. The inhibitory responses are always potentiated markedly by thiopentone but are affected in different ways by inhalational anaesthetic agents. The blockade of these inhibitory responses, noticed more frequently during the lighter stages of anaesthesia, might be related to the excitatory signs observed at times in clinical anaesthesia.[24]

Komatsu *et al.*[25] showed an unexpectedly high incidence of opisthotonus, often described as a broadly facilitated state of muscle stretch reflexes, in mice. A possible mechanism of opisthotonus during induction of anaesthesia in mice is that the higher centres are inhibited more rapidly

than the facilitatory cells of the reticular formation, eliciting stretch reflexes, and thereby resulting in opisthotonus. The activity of the facilitatory cells of the reticular formation may decrease as anaesthesia deepens, and the opisthotonus then disappears.

Drug-induced decerebrate rigidity provides an explanation for the wide range of unusual neurological sequelae of varying duration and intensity as well as prolonged, fluctuating and relapsing unconsciousness observed in these patients. Soliman and Gillies noted that muscle spasticity and response to painful stimulus coincided.[12] This reinforces the concept that somatosensory stimulation (tactile, visual or auditory) can augment the overactive stretch reflex and maintain the imbalance between the cortex and reticular formation. This is accentuated by a lowered reflex excitability, as observed in clinical decerebration[11] and it can be provoked simply by passive movement of an extremity. It would explain the susceptibility of the anxious unpremedicated patient. In drug-induced decerebrate rigidity, sleep depends primarily on the extent of the drug-induced imbalance between the cortex and reticular formation and secondarily on the level of somatosensory input. Case 1 had repeated neurological examinations and a wide range of investigations including blood sampling and lumbar puncture, which may have provided tactile stimulation sufficient to maintain decerebrate rigidity and its associated unconsciousness. Auditory stimuli to assess conscious level, and visual stimuli in the form of pupillary reaction to light and fundoscopic examination, would be contributory. Opisthotonic episodes in Case 1 coincided with measuring the blood pressure and testing the vestibulo-ocular reflex. A further lapse into unconsciousness associated with twitching 24 hours after operation occurred at the time of neurological assessment. In Case 3 episodes of myoclonic jerks one hour apart with associated loss of consciousness occurred against a background of consciousness and correlated with measurement of blood pressure and neurological assessment. Her lapses of unconsciousness would have resulted from enhanced decerebrate rigidity manifested as intense overactivity of the stretch reflex in the form of myoclonic jerks. In Case 2 consciousness was preserved but there was an inability to respond to verbal command or painful stimulus. Intense somatosensory stimulation was sufficient to maintain hypertonus but not sufficient to cause a critical level of decerebrate rigidity resulting in unconsciousness. In Case 4 opisthotonus again coincided with measuring the blood pressure. The airway may be compromised in opisthotonus and repeated efforts to insert an oropharyngeal airway or manipulate the jaw may be unnecessary as the episodes are often short-lived; indeed, such manoeuvres may provide the tactile stimulation to accentuate and prolong it.

A causal relationship between an anaesthetic agent and an adverse effect on the central nervous system requires exclusion of physical predisposition (epilepsy), disease (sepsis), pyrexia, cerebral pathology and metabolic abnormality. In the first three cases a range of biochemical tests including thyroid function tests were performed and were normal. The first two cases were on the same operating list and contamination of the anaesthetic agents with impurities or drugs with known established adverse effects on the CNS, or faulty anaesthetic equipment resulting in toxic doses of these anaesthetic agents, were considered. Enflurane drained from the vaporizers, propofol from broken ampoules and the remaining batch, and nitrous oxide cylinders were sent to the manufacturers for quality control; all analyses were normal. The vaporizers and anaesthetic machines were tested. Electroencephalographs performed in the first three cases showed a sleep-like pattern consistent with cortical depression and no evidence of epileptiform activity; this is consistent with drug-induced decerebrate rigidity.[23] Enflurane produces characteristic changes on EEG which are known to increase with depth of anaesthesia or change in $Paco_2$, and may persist for 30 days after administration.[26] These EEG changes are associated with a spectrum of neurological sequelae from myoclonic jerks to epileptic seizures.[27] The first three patients were assessed by a neurologist and he was able to observe and define opisthotonus and myoclonus. Thus an accurate description of the clinical findings provided a stronger basis to support the concept of drug-induced decerebrate rigidity in these patients.

Excitatory effects, particularly in unpremedicated patients, are observed frequently on induction of anaesthesia with well established anaesthetic agents such as methohexitone and etomidate, and manifest as hypertonus, twitching and tremor.[28,29] Excitatory effects of methohexitone have been used to activate abnormal EEG tracings.[28] Similar muscle movements have been observed recently in association with the use of propofol but the extent of the muscle movement was noted to be much smaller.[30] The origin of these excitatory effects within the neuro-axis depends on the excitatory and depressive effects of the anaesthetic agents on neurones located in the cortex, thalamus and reticular formation.[31] However, it must be emphasised that they have a common path which results in facilitation of the anterior horn cells. The majority of adverse CNS effects in which propofol was implicated occurred in the recovery phase and these result probably from the same mechanism that causes excitatory changes on induction. Again, the anxious, unpremedicated patient who undergoes a short painful procedure is more susceptible to the adverse effects of propofol on emergence from anaesthesia.

Day-case surgery has become increasingly popular, partly because of technical advances in surgery that allow shorter and less invasive procedures and partly as a result of the introduction of anaesthetic agents that allow more rapid recovery. However, adverse CNS effects attributed to propofol have implications in day-case surgery where emphasis is on minimal morbidity. A lack of knowledge of the neurophysiological basis of anaesthesia, along with a lack of awareness of, and inability to detect and diagnose, adverse CNS effects related to anaesthesia may result in misguided reporting and under-reporting to the CSM. An adverse CNS effect related to an anaesthetic agent may be attributed to pre-existing neurological disease rather than the anaesthetic agent. Twitching may be mistaken for residual neuromuscular blockade and thus treated inappropriately. Adverse CNS effects which are brief or infrequent and associated with no subsequent morbidity may not be observed or reported, and there may be uncertainty as to which drug to report. The CSM Adverse Drug Analysis Information Service gives guidelines for all new drugs: 'Report all suspected reactions, that is, any adverse or untoward event, however minor, which could conceivably be attributed to the drug. Please report even if you are unsure of causal relationship or if the reaction is well

recognised'.[32] It is probably coincidental that there were two adverse CNS effects in consecutive patients on the same operating list and this implies a much higher incidence than reports to date have suggested. A delay in recovery may be considered not unusual, but if the technique is routine and most of the patients recover quickly then it is perhaps 'untoward'. A number of these reactions may occur in the same patient e.g. twitching, opisthotonus and prolonged unconsciousness. It is obviously important to emphasise the correct primary reaction. In addition, the adverse CNS effect may be misdiagnosed; for example, opisthotonus may be confused with oculogyric crisis, or myoclonus with loss of consciousness may be interpreted as a grand mal seizure. In both cases the implications are quite different.

A wide range of neurological sequelae after propofol have been described and some of these may have been classified and treated inappropriately. Our neurophysiological understanding of drug-induced decerebrate rigidity implies cortical depression and without confirmatory EEG evidence of epileptic discharge the term 'seizure' commonly used in similar reports may be inappropriate.[10,15] Epileptiform movement would not have the same connotation. Myoclonic activity is known to occur at different levels of the neuro-axis.[17,29] The drug should still be used with care in epileptics, but on the basis that such patients are more susceptible to drug-induced decerebrate rigidity.[28]

The CSM also drew attention in its most recent statement to reports of eight patients who either had a delay in regaining consciousness after propofol anaesthesia (over one hour) or who initially awoke but subsequently lapsed into unconsciousness. They noted that a large proportion of these patients had undergone investigative procedures or minor surgery. They advised that an adequate period of recovery must be allowed before discharging patients after day-case surgery.[6] The discharge of patients from day-case surgery adheres to strict guidelines. Drug-induced decerebrate rigidity and any accompanying loss of consciousness present usually in the early recovery period and, with prompt recognition, should be self-limiting. An appropriate time of discharge can be determined by resolution of the clinical signs of this condition.

Awareness associated with an ability to respond to verbal command or painful stimulus as described in Case 2 is consistent with decerebrate rigidity.[11] Failure to recognise this may result in considerable anxiety to the patient and possible medicolegal implications.

Adverse effects are well described with all currently used intravenous anaesthetic agents. The adverse CNS effects attributed to propofol have wide ranging implications. It is difficult to suggest specific restrictions for the use of propofol, unless a neurophysiological basis can be established. Convulsions related to anaesthesia raise a number of issues because their misinterpretation may result in patients being treated and labelled as 'epileptic'. Understanding and recognition of propofol-induced decerebrate rigidity, a self-limiting condition, may help to resolve these confusions. Propofol perhaps should be avoided in anxious or epileptic patients particularly when undergoing short procedures, but further restrictions can be established only if an analysis of the CSM reports of adverse CNS effects related to propofol is performed, taking into account a wide variety of factors, so that we can gain a clearer understanding of the correct role of this drug in the future.

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CASE REPORT

An unusual complication of tracheal intubation

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Summary

We report a previously undescribed complication of tracheal intubation. The complication arose as a result of tracheal intubation performed as an emergency procedure in a patient with an abnormal anteriorly placed larynx. Subsequent corrective laryngeal surgery was required after a temporary tracheostomy had been performed.

Key words

Intubation, tracheal; complications.

Case history

A 39-year-old male psychiatric social worker suffered an influenza-like illness whilst on holiday in Greece. He complained of a number of nonspecific neurological symptoms that included light headedness, blurring of vision and generalised headaches, during the next 6 weeks. He presented to his general practitioner, who found his blood pressure to be 200/130 mmHg. He was transferred immediately to his local hospital for treatment and investigation of hypertension.

Whilst in hospital, he received dextromoramide 10 mg orally for his headache, which had not responded to simple analgesics. He suffered a respiratory arrest one hour after administration of the drug. Subsequent tracheal intubation required multiple attempts, since visualisation of the vocal cords was found to be impossible because of a very anteriorly situated larynx.

The patient was weaned from ventilatory support and his trachea was extubated after resuscitation and a period of elective ventilation on the intensive care unit. He complained of some difficulty in breathing after extubation and said that there seemed to be an 'increased resistance' to both inspiration and expiration. It became apparent that he was having periods of apnoea, especially whilst asleep. Sleep studies confirmed frequent episodes of mixed central and obstructive apnoea during which arterial oxygen saturation decreased to between 60 and 70%. Indirect laryngoscopy revealed a medially displaced right arytenoid cartilage which partially obstructed the laryngeal inlet and accounted for the increased resistance to breathing and the obstructive component of the sleep apnoea.

Flow volume loops were performed and revealed a normal forced vital capacity (FVC) with a 14% reduction in FEV_1/FVC ratio from normal and a peak expiratory flow rate (PEFR) of 55% of the predicted value. In addition, the expiratory curve demonstrated an abnormal 'dip' during early expiration, which indicated obstruction to air flow.

Direct laryngoscopy was attempted under general anaesthesia but was abandoned because only a limited view of the larynx was obtained. It was decided that a tracheostomy was required to relieve the laryngeal obstruction and to facilitate nocturnal positive pressure ventilation.

Neurological investigation had provided a diagnosis of Lyme disease, a tick-borne spirochaetal infection which, on occasions, may produce a variable encephalitis.[1] Magnetic resonance imaging revealed a lesion in the brain stem which presumably affected the tractus solitarius and accounted for the central sleep apnoea and the labile hypertension.

Corrective surgery of the larynx was carried out at a later date through a transcutaneous incision. It was found at operation that the junction between the inferior aspect of the right arytenoid and the cricoid cartilages was disrupted, with the formation of pseudarthrosis. The posterior cricoarytenoid ligament was found to be torn, and the right arytenoid cartilage was displaced and fixed medially and partially obscured the laryngeal inlet. The right arytenoid cartilage was therefore resected.

The patient underwent a further sleep study 4 weeks

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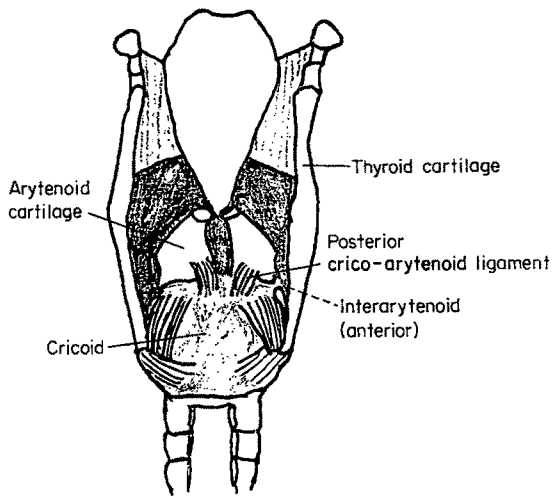

Fig. 1. The posterior aspect of the larynx.

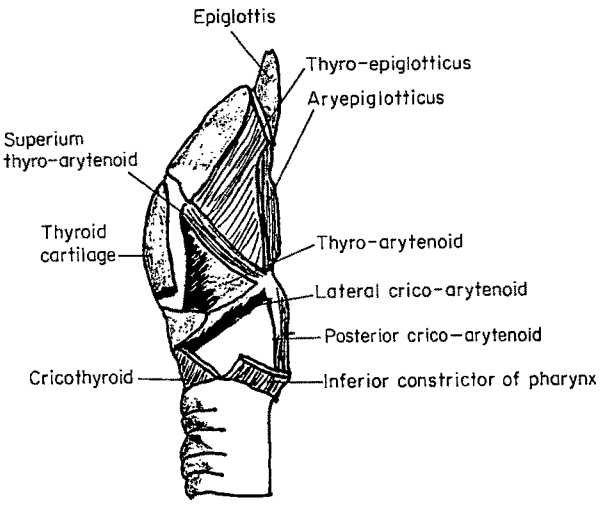

Fig. 2. The muscles of the larynx, left lateral aspect.

after the operation, during which his tracheostomy was occluded. Analysis showed complete resolution of his central and obstructive sleep apnoea. Primary closure of the tracheostomy was therefore carried out. Postoperative flow-volume loops showed a normal expiratory curve. The FVC was largely unchanged, but the FEV_1/FVC ratio was within 1% of the predicted value. He has since made a full recovery.

Discussion

Significant trauma to the larynx during attempted tracheal intubation is well recognised,[2] and its incidence was reported to be as high as 6.2%.[3] However, complete disruption of the crico-arytenoid joint has not been described before.

The inferior aspect of the arytenoid cartilage forms a synovial joint with the cricoid cartilage. The joint capsule is lax and allows a wide range of movement. Stability is provided by the posterior crico-arytenoid ligament while mobility of the arytenoid is controlled by seven individual muscles (Figs 1 and 2). The interplay of these muscles allows movement of the arytenoid cartilage on its fulcrum—the crico-arytenoid joint. If the posterior crico-arytenoid ligament is disrupted, stability of the joint is lost and traction of the lateral crico-arytenoid, the interarytenoid and the thyro-arytenoid muscles tends to displace the arytenoid cartilage medially and downwards, and obstruct the laryngeal inlet.

A number of factors could have contributed to the damage to the posterior crico-arytenoid ligament in our patient. The extreme anterior position of the larynx made visualisation of the vocal cords impossible and attempts at intubation directed the tracheal tube towards the posterior aspect of the larynx. There are several possible mechanisms to explain the damage caused to the posterior crico-arytenoid ligament. The tracheal tube may have been passed into the right piriform fossa and any excessive force applied may have caused medial displacement of the arytenoid cartilage. Alternatively, the corniculate cartilage at the apex of the arytenoid may have become incorporated within the lumen of the tracheal tube whereupon any attempt to advance the tube would result in displacement of the arytenoid cartilage. In addition, the intubation was performed as an emergency and hurried attempts at placing the tracheal tube with poor positioning of the patient may have resulted in the tube being directed posteriorly.

There have been a number of previous reports of simple dislocation of an arytenoid cartilage associated with laryngoscopy and tracheal intubation.[4–9] These dislocations have all been reduced by simple counterpressure under direct laryngoscopy performed under either local or general anaesthesia. One patient underwent computed tomography to confirm the diagnosis.[4] In only one instance was the resultant reduction deemed to be incomplete and the patient was due to undergo either Teflon injection of the affected vocal cord, or surgical reconstruction of the crico-arytenoid joint.[5]

The place of surgery in restoration of the crico-arytenoid joint is said to be disappointing in that it leaves an unphysiological larynx with alteration of voice and the continued risk of aspiration of fluids and poor cough effort.[6]

One of the patients described[7] was an acromegalic, and the cause of dislocation was thought to be degeneration of the crico-arytenoid joint ligaments, associated with the acromegalic disease process. Laxity of the ligaments could not be attributed to any chronic underlying disease in the remainder.

The presenting features in three of these patients[8] included pain on swallowing either liquids or solids, while all of the patients complained of a sore throat and weak voice. There was a variable delay of between 2 days and 3 weeks before patients were investigated for their symptoms. The reasons stated for the delay were the presence of a nasogastric tube that caused pain on swallowing and sore throat, and the presence of laryngeal oedema that resulted in pain and hoarseness of voice. These two factors may cause the symptoms experienced by the patients, but they do not exclude the possibility of other pathology. Some of the patients were not investigated until they developed an aspiration pneumonitis from laryngeal incompetence and poor effort of cough.

The suggested mechanisms of damage were varied. Only one intubation was described as traumatic and difficult.[8] Some patients had undergone tracheal intubation on several occasions for repeated surgical procedures while others were intubated for prolonged periods of time—up to 11 days; in that case it is suggested that continual move-

ment of the head may have led to dislocation of the arytenoid after extubation.[5] The same author suggests that laryngoscopy itself may be responsible for exposing the larynx to trauma during insertion of the tracheal tube. The aryepiglottic folds are stretched during laryngoscopy and produce an upward and outward pull on the arytenoid cartilages which are drawn laterally. This places the left arytenoid in such a position that it may be dislocated by the passage of a tracheal tube passed from the right. We suggest that such damage is as likely to the right arytenoid, as we have described.

Dislocation and displacement of the arytenoid cartilage, although extremely rare, should be considered in the differential diagnosis of any patient who complains of 'difficulty in breathing', after tracheal extubation.

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CASE REPORT

Respiratory tract infection and anaesthesia

Haemophilus influenzae pneumonia that developed under anaesthesia

N. N. CAMPBELL

Summary

A 2-year-old boy with symptoms of a minor upper respiratory tract infection developed Haemophilus influenzae pneumonia that presented as hypoxaemia under anaesthesia for minor emergency surgery. The patient required 72 hours of mechanical ventilation in an intensive care unit after the anaesthetic and thereafter made an uneventful recovery. The value of pre-operative chest radiology and the possible contributory effect of anaesthesia are discussed.

Key words

Anaesthesia; paediatric.
Infection; pulmonary.

A 26-month-old boy sustained a 1-cm cut to his upper lip after a fall at home. It was decided to suture the laceration under general anaesthesia. The child had been previously healthy, though for the past 4 days suffered from an upper respiratory tract infection. Physical examination revealed an apyrexial child with a runny nose and a slight, nonproductive, cough. Auscultation of the chest was normal. It was considered that in view of the mild nature of the respiratory signs and symptoms it was reasonable to proceed with general anaesthesia after a total period of 6 hours starvation.

No premedication was given except for EMLA cream to the dorsum of both hands. Anaesthesia was induced in the anaesthetic room with thiopentone via a 22-gauge cannula in the dorsum of the left hand, and atracurium was given to facilitate intubation and ventilation. Manual inflation with a mask was uneventful before tracheal intubation. He was intubated with a 4.5-mm uncuffed tracheal tube which was changed to a 4.0-mm tube to achieve a slight leak. Some clear pharyngeal secretions were aspirated during the change of the tube. It was noticed that the chest was less compliant than might be expected and the position of the tube was checked to exclude bronchial intubation. The tube was secured in position. An Ayre's T-piece and manual ventilation were used throughout.

The patient was then transferred to theatre where marked asymmetry of chest movements was noticed; the right lung appeared barely to inflate. Chest compliance remained poor. The child was cyanosed with a rapidly decreasing oxygen saturation. Oxygen 100% was administered and the tracheal tube removed and mask ventilation performed. The oxygen saturation improved although it was still only 90% and inflation of the right lung was still limited. The trachea was reintubated with great care to ensure no bronchial placement of the tube. Auscultation of the lungs revealed coarse crepitations in the right lung. The oxygen saturation was 85–90% with an F_{IO_2} of 1.0. Surgery was completed rapidly and a chest X ray requested. The child was sedated and paralysed with intermittent injections of propofol and atracurium.

The chest X ray showed loss of volume in the whole right hemithorax with consolidation of the right upper lobe and compensatory emphysema in the left lung. The tracheal tube was correctly positioned. The differential diagnosis at this stage was a foreign body in the right main bronchus or an aspiration pneumonitis. There had been no clinical evidence of regurgitation and the pharyngeal aspirate was alkaline on testing with litmus paper. A small amount of clear fluid was aspirated from the stomach. Dentition was intact. It was decided, after discussion with the radiologist and ENT surgeon, to perform a rigid bronchoscopy. This was performed with a ventilating bronchoscope. The trachea and both bronchi were normal without evidence of a foreign body, aspirated material or pus. A chest X ray performed at this stage showed that in addition to right upper lobe consolidation there was bilateral basal shadowing.

The tracheal tube was reintroduced through the nose and the patient transferred to the paediatric intensive care unit for ventilatory support and further management. The

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oxygen saturation was 90–95% with an F_{IO_2} of 1.0. Peak airway pressures of 3.0 kPa indicated poor compliance. Blood cultures were taken. A tracheal aspirate sent for urgent microscopy revealed pus cells, gram-positive cocci and scant gram-negative bacilli. Flucloxacillin and netilmycin were started. Culture of the tracheal aspirate revealed a moderately heavy growth of *Haemophilus influenzae*. The blood cultures were sterile. Ampicillin was added to the therapeutic regime.

The patient required mechanical ventilation for 3 days and the pneumonia gradually improved. Chest X ray taken 5 days after the event showed some remaining right upper lobe shadowing but the consolidation had resolved, as had the basal shadowing. He was discharged from hospital.

Discussion

Haemophilus influenzae is a common cause of serious bacterial infection in infants and children. Nasopharyngeal infection precedes almost all clinical varieties of localised disease such as pneumonia. The onset is often insidious and the course prolonged over several weeks. A cough is almost always present but may not be productive. The pneumonia is usually lobar but there is no characteristic radiological feature.[1]

The patient in the case described had many of the typical features of an early *Haemophilus influenzae* infection—a mild rhinnorhoea and nonproductive cough but without general malaise. Unfortunately these symptoms are both nonspecific and common in young children and are usually associated with a viral upper respiratory tract infection (URTI). The evidence to support increased morbidity in patients with a recent or current URTI is tenuous. Indeed, a study of 489 children with URTI who had elective myringotomy demonstrates the prevalence and duration of respiratory symptoms to be significantly less postoperatively than in matched controls.[2] By contrast the severity of oxygen desaturation in the immediate postoperative period in children with a recent URTI has been shown to be greater than in those without such symptoms unless supplemental oxygen is given.[3] This patient required emergency surgery so it was necessary to proceed despite the respiratory symptoms.

It is debatable whether a pre-operative chest X ray should have been performed. The radiologist commented that the initial X ray changes were typical of more long-standing pulmonary collapse than would have occurred in the hour from induction of anaesthesia to when the X ray was performed. This would seem to indicate that a pre-operative chest X ray might have provided useful information. The Royal College of Radiologists have produced clinical guidelines for the use of pre-operative chest X ray among patients admitted for elective surgery.[4] These include those with acute respiratory symptoms. However, both the admitting surgeon and the anaesthetist had found the chest normal to auscultation before operation and it would be inappropriate to perform a chest X ray in all children with the symptoms and signs described in this case.

It is known that the immune response is altered by surgery and anaesthesia. Specific immunity is depressed with a reduction in B-lymphocyte numbers and in antibody production. T-lymphocyte responsiveness has been shown to be depressed after anaesthesia and before the start of surgery. Tracheal mucociliary flow is decreased by anaesthesia as is pulmonary bactericidal activity.[5] The rapid exacerbation of this pneumonia may, in part, be attributable to these changes. It is possible that the positive pressure ventilation may have aided spread of bacteria from the upper to the lower respiratory tract. This case illustrates an unfortunate coincidence of the need for emergency surgery at the very time that a *Haemophilus influenzae* pneumonia was developing. The induction of anaesthesia and tracheal intubation were chronologically linked to the sudden deterioration in the child's condition. The prediction of problems is not always possible despite apparently satisfactory pre-operative assessment. Pre-operative chest X ray in all children with upper respiratory symptoms is not usually indicated, but there may be times when this would be informative, particularly if cough is a prominent symptom.

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APPARATUS

Maintenance of body temperature in elderly patients who have joint replacement surgery

A comparison between the heat and moisture exchanger and heated humidifier

P. C. Ip Yam and F. Carli

Summary

The effect of a heat and moisture exchanger on intra-operative aural canal (core) and mean skin temperatures was investigated in elderly patients who had elective total hip arthroplasty under general anaesthesia with artificial ventilation of the lungs. Group 1 ($n = 20$) did not receive any form of artificial humidification while in group 2 ($n = 20$) a heat and moisture exchanger was inserted in the breathing system and in group 3 ($n = 20$) the inspired gases were humidified and warmed at 40°C by means of a heated humidifier. Time of surgery, intravenous fluid administration and operating theatre temperature were standardised. Mean (SD) aural canal (core) temperature decreased significantly in groups 1 and 2 ($p < 0.001$), while there was a fall of 0.3°C(0.6) in group 3, which was not significant. Mean skin temperature decreased during anaesthesia and surgery in both groups 1 and 2 ($p < 0.05$), while it increased in group 3. There was a significantly greater loss of body heat in groups 1 and 2 compared with group 3 intra-operatively ($p < 0.001$). We conclude that a heat and moisture exchanger did not prevent the decrease in intra-operative body temperature in elderly patients.

Key words

Temperature; body, monitoring.
Hypothermia; intra-operative.

Loss of body heat during anaesthesia and surgery can occur as a result of low ambient temperature, ventilation of the lungs with cold gases, drug-induced vasodilatation and administration of cold intravenous fluids.[1] Maintenance of body temperature during prolonged surgery in an elderly population demands careful consideration. These patients have limited physiological and cardiorespiratory reserves and are at a greater risk from the metabolic demands incurred by hypothermia in the immediate period after operation.[2,3]

Single-use condenser heat and moisture exchangers (HME) have recently received attention since they are capable of maintaining high inspiratory humidity.[4] The few clinical investigations undertaken to assess their usefulness in maintaining body temperature during anaesthesia and surgery have given conflicting results.[5,6]

The aim of the present study was to compare intra-operative changes in body temperature and heat loss between groups of elderly patients who received fresh gases humidified via either HME or a heated humidifier. The operative procedure, type of patients studied and theatre temperature were standardised.

Patients and methods

Sixty elderly patients scheduled for elective total hip arthroplasty for osteoarthritis were studied. The investigation was approved by the Hospital Ethics Committee and informed consent was obtained. Patients who were grossly obese or who suffered from endocrine diseases were excluded, as well as those with pyrexia.

Premedication consisted of intramuscular papaveretum and hyoscine. General anaesthesia was induced with thiopentone; the trachea was intubated after administration of pancuronium bromide, and anaesthesia was supplemented with enflurane (end-tidal concentration 1.67(0.31)%). The patients' lungs were ventilated to normocapnia with a mixture of 70% nitrous oxide in oxygen. Fresh gas flow rates were between 80 and 100 (ml/kg)/minute.

Patients were allocated randomly to three groups of 20: group 1 to act as control, with no form of artificial humidification; group 2 to have a HME (Thermovent 1200, Portex) next to the tracheal tube and group 3 to receive warmed and humidified gases to 40°C by means of a heated cascade water humidifier. The temperature of the heated

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inspiratory gases was monitored by means of a thermocouple at the patient's airway. Compound sodium lactate was administered intravenously at 6 (ml/kg)/hour at room temperature. Blood, when required, was warmed to 37°C before infusion.

Skin surface thermocouple probes were placed against the lateral aspect of the upper arm, the nipple, the ventral surface of the mid thigh and the lateral aspect of the calf. Another temperature probe was inserted under direct vision in the aural canal and well secured with cotton wool. Surface skin and aural canal (core) temperature measurements were recorded at induction of anaesthesia and at the end of the surgery, before reversal of muscle relaxant. The thermocouple probes and the recording thermometer (Comark Electronics) were calibrated against a National Physics Laboratory mercury-in-glass thermometer and found to be accurate to within 0.1°C.

Mean skin temperature (Tskin) was derived using Ramanathan's four-point formula:[7] 0.3 (nipple temperature + arm temperature) + 0.2 (thigh temperature + calf temperature). Mean body temperature (Tm) was calculated using the formula of Colin and others:[8] 0.66 (aural canal temperature) + 0.34 (mean skin temperature). Change in mean body heat content was then derived: $Tm \times 0.83 \times 4.18$ where 0.83 represents specific heat. The operations were performed in a designated orthopaedic theatre with controlled laminar flow where relative humidity was maintained between 40 and 50% and ambient temperature set between 19 and 21°C. All patients were in a supine position and covered with a gown and standard sterile drapes. All patients at the end of surgery were transferred to the recovery room where the incidence of shivering was noted by the nursing personnel.

Statistical analysis

The temperatures at the beginning and end were grouped and the mean values and standard deviations were derived for each group. Student's paired *t*-test was used to compare observations within the same group of patients and unpaired *t*-test, or Welch's test where appropriate, for comparison among different groups. Values of $p < 0.05$ were considered significant.

Results

There were no significant differences between the three groups with regard to the patients' physical characteristics and duration of surgery (Table 1). Mean (SD) ambient temperatures during the study were 20.2°C (1.1) (group 1), 20.5°C (0.8) (group 2) and 19.8°C (0.8) (group 3). Blood was administered in six patients in group 1, seven in group 2 and seven in group 3.

Table 1. Anthropometric characteristics of the patients studied, duration of surgery and incidence of shivering.

Mean (SD)	Group 1 ($n=20$)	Group 2 ($n=20$)	Group 3 ($n=20$)
Age (years)	73 (8)	70 (6)	68 (9)
Weight (kg)	69 (10)	64 (8)	63 (13)
Height (cm)	162 (10)	160 (4)	165 (6)
Males : females	6 : 14	3 : 17	8 : 12
Duration of surgery (minutes)	127 (40)	128 (36)	133 (44)
Incidence of shivering (n)	10	8	4

Table 2. Aural canal temperatures (°C).

Mean (SD)	Group 1 ($n=20$)	Group 2 ($n=20$)	Group 3 ($n=20$)
Before anaesthesia	36.1 (0.7)	36.1 (0.6)	36.1 (0.5)
End of surgery	34.9 (0.7)*	34.8 (0.6)*	35.8 (0.7)
Change (°C)	−1.3 (0.7)†	−1.2 (0.9)†	−0.3 (0.6)

*$p<0.001$ compared with before anaesthesia (paired *t*-test).
†$p<0.001$ compared with group 3 (unpaired *t*-test).

There was no difference in aural canal temperatures between the three groups of patients at induction of anaesthesia (Table 2). Mean aural canal temperature decreased significantly during anaesthesia and surgery in groups 1 and 2 ($p < 0.001$ by paired *t*-test) whereas no significant change occurred in group 3 (Table 2). The change in aural canal temperature in the latter group (0.3°C (0.6)) was significantly less than the other two groups ($p < 0.001$ by unpaired *t*-test). There was no significant difference between groups 1 and 2.

There was no difference in mean skin temperatures between the three groups at induction of anaesthesia (Table 3). Mean skin temperature decreased significantly during anaesthesia and surgery in groups 1 and 2 ($p < 0.05$ by paired *t*-test). In contrast, mean skin temperature in group 3 showed a significant increase ($p < .001$). Mean body heat content decreased by the same amount in groups 1 and 2, whereas in the heated humidifier group it was retained. (Fig. 1.)

The incidence of shivering in groups 1 and 2 was higher than in group 3.

Discussion

The results of this study show that HME did not prevent the decrease in core and mean skin temperatures during anaesthesia in a group of elderly patients who had hip surgery. The intra-operative loss of body heat was similar to that of a control group. The decrease in core temperature was minimal (0.3°C) while mean skin temperature increased when a heated water humidifier was inserted in the system and the fresh gases warmed at 40°C.

The HME is a cheap and attractive device with the advantage of simplicity. Tests on artificial test rigs demonstrate its ability to retain moisture and heat.[4] Bench tests, however, have shown that the HME is unable to provide as much heat and moisture to inspired gases as heated humidifiers.[9] This is confirmed in the present investigation where the heated humidifier group retained heat while HME and

Table 3. Mean skin temperatures (°C).

Mean (SD)	Group 1 ($n=20$)	Group 2 ($n=20$)	Group 3 ($n=29$)
Before anaesthesia	32.8 (1)	32.3 (1.3)	31.9 (1)
End of surgery	32.4 (0.8)*	31.9 (1)*	32.7 (1.1)†
Change (°C)	−0.4 (0.6)‡	−0.5 (1)‡	+0.7 (0.5)

*$p<0.05$.
†$p<0.001$ compared with before anaesthesia (paired *t*-test).
‡$p<0.001$ compared with group 3 (unpaired *t*-test).

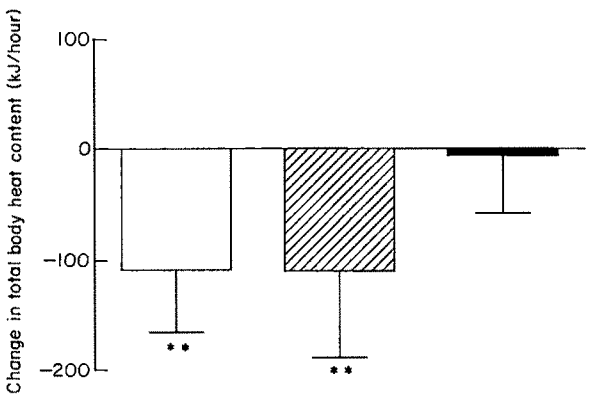

Fig. 1. Intra-operative changes in body heat content in the three groups studied. Data are presented as mean (SD). There was a significant difference between the heated group (■) and the control (□) and HME (▨) groups ($p < 0.001$).

control groups cooled significantly. There are few controlled studies which examine the ability of the HME to maintain body temperature in a clinical setting. Chalon *et al.*[10] investigated 10 patients who had upper and lower abdominal surgery, and reported that in operations that lasted 150 minutes the use of an HME contributed significantly to maintenance of body temperature. However, in their investigation the authors standardised neither age, type of surgery nor environment. The patients studied were in addition wrapped in cotton blankets which might have minimised radiant heat loss.

The degree of cooling might in part be related to the fresh gas glow rates used during anaesthesia. Haslam *et al.*[6] reported that, by using the low flow rates (3 litres/minute) of fresh gases in conjunction with an HME, body heat conservation was better than when high flow rates (6 litres/minute) were used. However, this contention was not supported significantly by their data. The mean decrease in core temperature observed in those patients who received 6 litres/minute of fresh gas flow with an HME was less than that that occurred in group 2 of our study for the same duration of anaesthesia and surgery (0.7 compared with 1.2°C). We do not know the reason for this discrepancy; perhaps much younger subjects were studied.

The technique of heating and humidifying fresh gases to 37°C and 100% relative humidity, as applied in the present study, was shown to limit hypothermia in anaesthetised patients.[11–13] However, maintainance of normothermia can be achieved fully only when warming blankets and blood warmers are also used. The small decrease in aural canal temperature in group 3 of our study was associated with an increase in mean skin temperature. This might be explained by the distribution of heat from the core to the periphery and limited evaporative loss from the small exposed area.[14]

In conclusion, we were not able to demonstrate any advantage in using the HME to maintain normothermia in elderly patients who had hip replacement surgery that lasted 2 hours in a cold operating theatre. A heated humidifier as a means of counteracting intra-operative heat loss could be a practical solution.

Acknowledgments

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REVIEW

Postoperative hypoxaemia: mechanisms and time course

J. G. JONES, D. J. SAPSFORD AND R. G. WHEATLEY

Summary

Postoperative hypoxaemia results predominantly from two mechanisms. Gas exchange is impaired during anaesthesia as a result of reduced tone in the muscles of the chest wall and probably alterations in bronchomotor and vascular tone, and the resulting changes persist into the postoperative period. In addition, there is an abnormality of control of breathing, which results in episodic obstructive apnoea. These episodes continue for several days after operation and are related to sleep pattern and analgesic administration, although the precise effects of different analgesic regimens have not been evaluated. Oxygen administration is effect in reducing the degree of hypoxaemia.

Key words

Hypoxia; postoperative.
Lung; atelectasis.

The role of intra-operative atelectasis

It is widely believed that postoperative respiratory depression after administration of opioid is a rare event.[1] However, the validity of this belief depends on the criteria used to define respiratory depression. Most investigators have focused on hypercapnia or changes in ventilatory rate as the main indicators of postoperative respiratory depression. We showed recently that 60% of patients who received a morphine infusion after operation had episodes of hypoxaemia ($Spo_2 < 80\%$). These were associated with obstructive apnoea, occurred exclusively during sleep and were rarely associated with a slow respiratory rate or small tidal volume.[2] It must be emphasised that hypoxaemia rather than hypercapnia is of the greatest clinical concern, but the degree of hypoxaemia has, until recently, rarely been measured in postoperative patients. General anaesthesia, particularly for surgical procedures on the upper abdomen and thorax, is followed by a decrease in Pao_2 which may persist for many days postoperatively. This is caused by intrapulmonary shunting and is less frequently accompanied by either a change in $Paco_2$ or reduced rate of breathing. An explanation for this postoperative shunting is based on changes in lung function that are induced during anaesthesia and persist postoperatively. Postoperative opioid-induced obstructive apnoea leads to a further decrease in oxygen saturation. The problem is therefore the additive effect of two causes of hypoxaemia, each of which might be harmless, by itself.

The recent introduction of pulse oximetry has provided an excellent opportunity to examine in more detail the causes, severity and duration of postoperative hypoxaemia.

Mechanisms of impaired gas exchange during and after anaesthesia

One of the most consistent changes in pulmonary function after induction of anaesthesia is a reduction in functional residual capacity (FRC) due partly to a change in shape of the chest wall and partly to a change in intrathoracic blood volume. A close relationship has been shown between the reduction in FRC and an increase in alveolar–arterial Po_2 gradient.[3] Subsequent research has progressed in two directions: a search for the cause of the abnormality of gas exchange; and the cause of the change in lung volume.

The decreases in FRC and closing capacity. It was postulated that closure of basal airways was a consequence of the decrease in FRC and that the patients most likely to show this effect were those in whom the FRC and closing capacity, when awake, were very similar. A reduction in FRC after anaesthesia in such patients would move the end-expiratory point into the closing capacity, promote airway closure in the dependent lung and initiate a shunt or reduce ventilation/perfusion ratios. This turned out to be a rare event because there was often a comparable reduction in closing capacity after induction of anaesthesia[4] and thus many anaesthetised patients with impaired gas exchange

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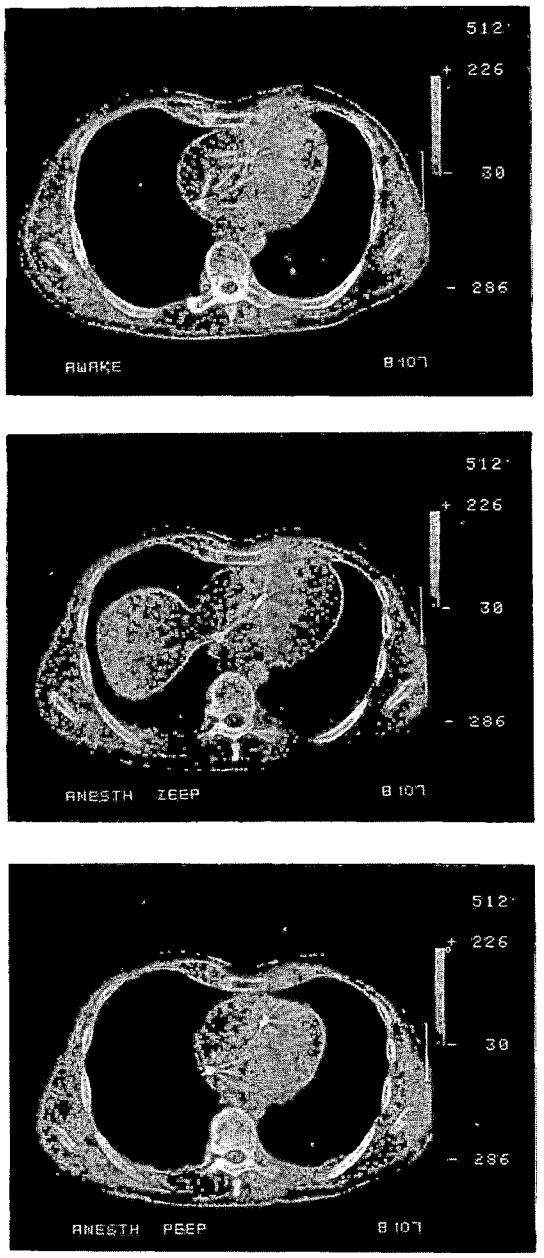

Fig. 1. Computerised tomographic scans of the chest before (awake) and during anaesthesia to show extensive dependent lung atelectasis during anaesthesia at zero end-expiratory pressure (ZEEP). Application of positive end-expiratory pressure (PEEP) reduced but did not abolish atelectasis. (The scans were kindly supplied to the author by Dr Hedernstierna.)

were not breathing within their closing capacity. However, it now seems likely that the closing volume test, which uses a sudden inflection in the expired tracer gas plateau, may not be a reliable test of basal lung atelectasis. Consequently, the relationship between a reduction in lung volume and a worsening of gas exchange must be re-examined.

Does increasing FRC reverse gas exchange abnormalities? Heneghan *et al.*[5] re-examined the causal relationship between changes in FRC and gas exchange in an attempt to answer this question. They showed that increasing FRC after induction of anaesthesia did not reverse the abnormal gas exchange and concluded that either the reduction in lung volume is not the cause of the gas exchange abnormality during anaesthesia, or that it is the cause but increasing lung volume does not reverse the effect. We will now consider these two hypotheses.

Hypoxic pulmonary vasoconstriction. It has been suggested in support of the first hypothesis that inhibition of hypoxic pulmonary vasoconstriction (HPV) by several general anaesthetic agents contributes to the worsening of gas exchange during anaesthesia. HPV normally directs blood away from the underventilated (low ventilation/perfusion) lung units with a resultant increase in Pa_{O_2} whereas persistence of flow to underventilated units causes the Pa_{O_2} to decrease.

The maximal effect of HPV occurs at a Pa_{O_2} of 4 kPa, when there is a 50% increase in vascular resistance. Thus, the compensating changes in perfusion are inadequate to preserve a normal ventilation–perfusion ($\dot{V}/\dot{Q}$) distribution for a very large reduction in ventilation, for example in atelectasis. HPV is lessened by anaesthetics but there is contradictory evidence as to the degree to which they attenuate this compensating response. There are also conflicting results of *in vivo* and *in vitro* animal studies in different species and in studies of anaesthetised humans.

Recent studies in man during one-lung anaesthesia show that adding 1 MAC of either halothane or isoflurane did not reduce Pa_{O_2} by impairing HPV. Eisenkraft[6] explains this lack of effect in terms of pre-existing vascular distension. If vascular pressure is normal there is little inhibition of HPV by anaesthetics whereas with a reduced vascular pressure, the inhibition of HPV is enhanced. This is a useful effect in terms of maintaining Pa_{O_2} but clearly it does not compensate for a reduced oxygen flux caused by a low cardiac output.

Eisenkraft[6] summarises the position as follows. HPV is directly inhibited by inhalational agents but in man the effect is of no clinical consequence. Thus, the inhibiting effect of HPV by general anaesthetics is clearly not the cause of oxygen desaturation, either during or immediately after anaesthesia.

Compromised airway function. What mechanisms explain the second hypothesis? Bendixen *et al.*[7] suggested more than 25 years ago the possibility of miliary atelectasis on the basis of a progressive decrease in lung compliance during anaesthesia, but conventional radiography has failed repeatedly to reveal such atelectasis. Nevertheless the scene is set for such collapse for the following reasons: lung volume is reduced during anaesthesia and airways narrow with reducing lung volume;[8] the dependent part of the lung shows the greatest degree of volume reduction and there is considerable impairment of movement of the dependent part of the diaphragm;[9] positive-pressure ventilation (or positive end-expiratory pressure) does not overcome the reduced movement of the dependent lung;[9] and positive end-expiratory pressure produces a much smaller degree of movement of the dependent diaphragm than phrenic nerve stimulation.[10] Dueck[11] has reviewed the recent literature on this subject. He points out that computerised tomography scans showed rapid development of dependent lung densities within 5–15 minutes of induction of anaesthesia.[12] These are presumed to be regions of atelectasis and their size correlates with the degree of intrapulmonary shunt.[13] Positive end-expiratory pressure (PEEP) of 1 kPa decreased the size of the atelectatic lung but did not eliminate the shunt (Fig. 1).

If a reduction in lung volume is associated with the development of atelectasis why does restoring lung volume to normal not restore normal gas exchange?

Dependent lung atelectasis and re-expansion. Studies of patients breathing halothane spontaneously via a mask showed less shunt and atelectasis, as well as lower $P(A\text{-}a)O_2$, than those whose trachea was intubated and who received muscle relaxants and mechanical ventilation.[14] It was found that the rib cage contribution to tidal volume was not suppressed in spontaneously breathing subjects, and FRC was unchanged from awake. However, intubated subjects showed a 20% reduction in FRC and a correspondingly increased $P(A\text{-}a)O_2$. This suggests that airway reflexes elicited by tracheal intubation may be a significant factor in anaesthesia-induced atelectasis.

A surprising finding[15] was that a 20% reduction in FRC due to chest wall restriction in healthy volunteers had no effect on shunt or $\dot{V}/\dot{Q}$ inequality. Dueck[11] speculated that the difference in shunt effects with anaesthesia compared with chest wall restriction is due in part to airway closure. Furthermore, the reduction in dependent regional lung volume during anaesthesia is associated with relaxation of the muscles of the chest wall and this is not simulated in awake subjects.

Strandberg *et al.*[13] reported that the atelectasis induced during anaesthesia could be demonstrated in 50% of patients 24 hours after completion of surgery. There is some reduction in the extent of atelectasis during the application of positive end-expiratory pressure, but the very low compliance of the atelectatic lung and the immobility of the adjacent part of the diaphragm prevent full expansion of the dependent lung. An important observation is that phrenic nerve stimulation partly overcomes this problem by recreating the tone and simulating the phasic activity which are impaired by anaesthesia.[10]

Thus there is now a convincing explanation of the gas exchange abnormality induced by anaesthesia based on atelectasis in the dependent part of the lung due to a reduction in FRC as well as reflex effects of tracheal intubation in closing small airways. The effects of this atelectasis on gas exchange are not reversed easily by passive lung inflation. However, it is worthwhile recalling that Browne *et al.*[16] showed that during one-lung anaesthesia the incidence of atelectasis was reduced by 50% when the anaesthetic mixture included 60% nitrogen and the role of nitrogen in anaesthetic gas mixtures should be re-examined. This may be an important factor in reducing the severity and duration of postoperative atelectasis and minimising the background hypoxaemia.

What causes the reduction in FRC? The reduction in FRC associated with general anaesthesia occurs whether the patient is paralysed or breathing spontaneously or whether anaesthesia is maintained by barbiturates or halothane. Ketamine and methohexitone are exceptional in that no reduction in FRC has been reported.[14,17]

A cranial displacement of the diaphragm was shown in anaesthetised patients[9] and was attributed to a reduction in tone in the diaphragm that is no longer able to oppose fully the hydrostatic pressure of the abdominal contents. It would be expected that the abdominal wall would be displaced inwards by an equal amount if the abdominal contents and diaphragm were moved up into the chest cavity. However, Jones *et al.*[18] found no change in either abdominal or rib cage circumference following induction of anaesthesia and suggested that a reduction of FRC could be explained in part by a central redistribution of blood volume. Hedenstierna *et al.*[19] used computed tomography to show that cranial shift of the diaphragm, reduction of FRC, and displacement of blood from thorax to abdomen occurred after induction of anaesthesia.

Abdominal distension (by blood or gastric balloon) causes a cranial shift of the diaphragm; however, in conscious subjects there is no reduction in FRC because of a compensatory outward movement of the rib cage. This important neural compensating mechanism is abolished during anaesthesia because of a reduction or even a loss of tone in the chest wall musculature. A similar mechanism would explain the reduction in FRC in obese patients, who are known to be at risk of complications during and after anaesthesia.

The other important factor is the shift in blood volume from the thorax and periphery to the abdomen. Hedenstierna *et al.*[19] suggested that the shift in blood volume is due to the increase in intrathoracic pressure that results from mechanical ventilation. A more attractive explanation is dilatation of the abdominal vasculature by halothane or enflurane,[20,21] or the central effects of anaesthetics which modulate autonomic control of the splanchnic circulation. This implies a shift in thoraco-abdominal blood volume as the cause of the change in FRC. In contrast, a change in thoraco-abdominal blood volume in conscious subjects does not change FRC because of compensatory changes in the tone of the chest wall musculature.

These studies lend considerable support to the hypothesis that a reduction in muscle tone in the chest wall is fundamental to the impairment of gas exchange during anaesthesia but that changes in bronchomotor and vascular tone may also play an important role.

Postoperative hypoxaemia

Early and late phases

The traditional view on this subject has been summarised by Craig[22] who considered postoperative hypoxaemia to occur in two phases: an early phase which may be due to anaesthetic drugs and techniques; and a late phase due to the administration of opioid drugs. He suggested that a low arterial oxygen tension is found immediately after anaesthesia and may last for up to 2 hours. This early hypoxaemia may be related causally to the anaesthetic itself, as it is an extension of the disorder of gas exchange that occurs during anaesthesia. Early postoperative hypoxaemia may be exacerbated by washout of nitrous oxide but a theoretical analysis suggests that N_2O elimination from the lung, in contrast to N_2O uptake, exerts a negligible effect on Pa_{O_2}.[23] It is our view that 'diffusion hypoxia' during nitrous oxide elimination is a unimportant.

The normal hypoxic drive to ventilation is abolished by concentrations of halothane and enflurane as low as 0.1 MAC.[24] These concentrations may be present during the immediate postoperative period and may explain some early phase respiratory depression. There is no strong evidence that this mechanism is important postoperatively.

Depression of ventilation after the administration of morphine and pentazocine lasts at least 7 hours in fit, young volunteers.[25] Fentanyl is claimed to be a much shorter acting analgesic although the duration of its respir-

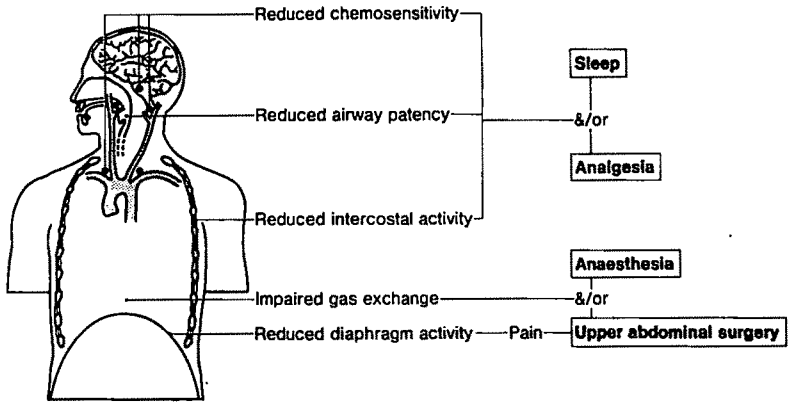

Fig. 2. This shows the interaction between anaesthesia, surgery, analgesia and sleep. (Reproduced by permission of *International Anesthesiology Clinics* and D.M. Catley, reference 30.)

atory and analgesic effects depends upon the dose administered, the effective volume of distribution and individual differences in susceptibility.[26] The problem of respiratory depression in the early postoperative phase is probably less of a hazard to the patient than that in the late phase because the level of observation and care is high during the period immediately after anaesthesia.

The early phase of impaired gas exchange is replaced by a later phase that may last up to a week after anaesthesia. This phase is more likely to occur after surgery on the thorax or upper abdomen, is more frequent in older patients and is characterised by a decrease in FRC to less than 60% of the pre-operative value.[27] It seems likely that the subdivision into early and late phases is artificial; there is a continuum of postoperative hypoxaemia which is more severe in some patients than others.

The decrease in lung volume is correlated with a decrease in Pa_{O_2}, although it is not known whether the former is caused primarily by changes in the chest wall or by mucous plugs and collapse of perfused alveoli. If severe restriction of chest movement by pain is an important cause, then it might be expected that adequate pain relief would abolish this effect.[28] Thoracic epidural analgesia was shown to produce complete pain relief but no change in FRC.[29] A possible explanation is that halothane may dilate splanchnic vessels and cause a central shift of blood volume which, in the supine position, displaces the diaphragm in a cephalad direction and reduces FRC. A similar mechanism is possible with epidural/spinal anaesthesia so that any tendency for FRC to increase because of analgesia is opposed by the reduction in FRC due to splanchnic vasodilatation.

Assessment of late phase effects

It is generally believed that the important respiratory side effects of opioid analgesics are slow ventilatory rate and diminished minute volume, and that these abnormalities are recognised easily on intermittent observation by nursing or medical staff. We used continuous respiratory monitoring techniques to demonstrate unpredictable and short-lived disturbances in ventilatory patterns during a postoperative study[28] in which the respiratory effects of continuous and intermittent opioid analgesia were compared. These disturbances were attributed to the effects of opioids and were not noticed by intermittent observation. Similar ventilatory disturbances are associated frequently with profound and potentially life-threatening hypoxaemia in patients with sleep apnoea syndrome. Anaesthesia and surgery commonly produce a background of mild hypoxaemia in the postoperative period; consequently, episodes of apnoea may result in profound decreases in arterial oxygen tension.

The interactions between anaesthesia, surgery, analgesia and sleep are summarised in Figure 2. This shows that there is a background of impaired gas exchange which causes intrapulmonary shunting as discussed above. This may be exacerbated by reduced movement of the chest wall as a consequence of postoperative pain. Against this background is superimposed an abnormality of ventilatory control due to the interaction of sleep and opioid analgesics. The effects of surgery and general anaesthesia on breathing patterns and oxygenation in the postoperative period were studied in two groups of patients who were monitored continuously overnight following surgery.[2] Each patient had received a standardised general anaesthetic and was recovering from either cholecystectomy or hip replacement. The patients were allocated randomly to receive postoperative analgesia with either regional analgesia with bupivacaine or an intravenous infusion of morphine over the subsequent 24 hours. The remarkable difference between the two groups of patients was the frequency of episodes of profound oxygen desaturation in the morphine group. Patients who received morphine had almost 500 episodes of marked oxygen desaturation ($Spo_2 < 80\%$) which occurred only when the ventilatory pattern was disturbed. In contrast, no patient in the postoperative regional anaesthesia group showed Sao_2 less than 87%, despite the fact that patients in this group also had apnoeic episodes.

There was a considerable reduction in arterial saturation after operation in both groups and this recovered towards normal over the subsequent 16 hours (Fig. 3). Sao_2 in the regional analgesia group was higher than in the morphine group. The episodes of hypoxaemia became less numerous throughout the night. There was a strong association between obstructive apnoea and hypoxaemia, and no episode of hypoxaemia was seen in association with central apnoea. All the hypoxaemic episodes ($Spo_2 < 80\%$) occurred during sleep and all in patients who received morphine.

It has been argued that central apnoea plays a role in the generation of obstructive apnoea and that central apnoea is

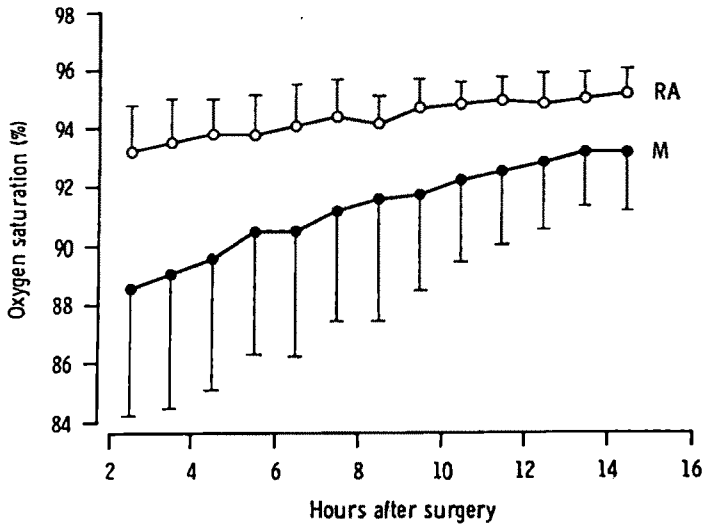

Fig. 3. Oxygen saturation was studied for 15 hours after surgery in two groups of patients breathing air. The oxygen saturation was reduced to a greater extent in patients who received intravenous morphine (M) than in those treated with regional anaesthesia (RA). Saturation in both groups recovers slowly towards the normal range but even after 14 hours the saturation is well below normal. (Reproduced by permission of *Anesthesiology* and D.M. Catley, reference 2.)

a manifestation of instability in the feedback control system which governs ventilation.[30] Hypoxaemia and hypercapnia stimulate chemoreceptors synergistically, causing an increased gain in the ventilatory control system. The combination of sleep, morphine and changes in circulation may lead to instabilities in the breathing pattern which manifest as sleep-related episodes of hyperventilation and apnoea. Furthermore, termination of periods of obstructive apnoea may be due to partial arousal achieved at specific levels of hypoxaemia. If this is true then the administration of oxygen would prolong the apnoeic period because a longer time would be required to achieve the arousal threshold of hypoxaemia.

Effect of oxygen administration

It is clear from the results of a subsequent study[31] that the administration of oxygen, while increasing oxygen saturation, had no beneficial effect on the number of periods of respiratory disturbance. It seems likely, therefore, that the hypoxaemia induced by morphine is not in itself an important cause of the apnoeic periods. A more likely explanation is that it is a direct effect of morphine, although such episodes in the postoperative period were seen in patients given regional anaesthesia for pain relief.[2] There was a gradual diminution in the time spent at low oxygen saturation during the 12-hour study period. This could be due to a waning of the effects both of the morphine loading dose and of the general anaesthetic itself. It is clear that at all times there was a beneficial effect of oxygen administration (Fig. 4).

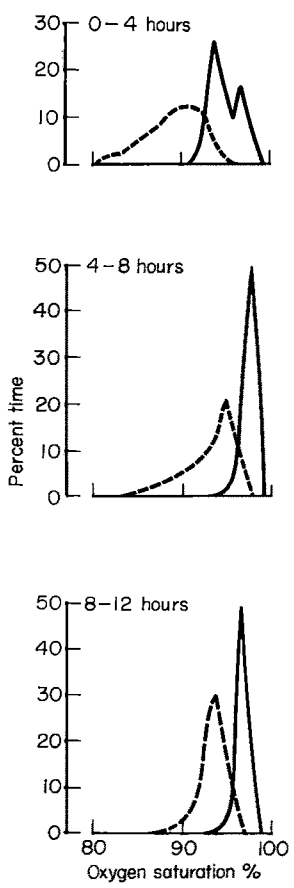

Fig. 4. The effect of oxygen administration on arterial oxygen saturation (Spo_2). The distribution of Spo_2 is plotted against % time. In each 4-hour period air (– – –) then 28% O_2 (———) was breathed, each for 2 hours. There is a higher Spo_2 in the period from 8–12 hours after operation than in the 0–4 hour postoperative period. (Reproduced by permission of *Journal of Royal Society of Medicine* and J.G. Jones, reference 31.)

Delayed hypoxaemia and REM sleep

There is an interaction between morphine analgesia and sleep in otherwise normal postoperative patients which

causes respiratory disturbances and episodes of hypoxaemia similar to those seen in patients with the sleep apnoea syndrome. In this condition, apnoeic episodes and oxygen desaturation occur during rapid eye movement (REM) sleep. However, we found that REM sleep did not occur on the night after surgery; this confirmed the findings of Aurell and Elmqvist.[32] Therefore the sleep apnoea induced by morphine after surgery occurs in the absence of REM sleep. However, it has been postulated that after REM sleep is abolished there is a 'catching up' period during which, in subsequent nights, there is prolonged REM sleep with an increased tendency to REM-associated sleep apnoea. Knill (personal communication) has shown that on the third night after surgery the most profound episodes of hypoxaemia occur, all entirely during REM sleep. Other authors[32] have shown gross disturbances of sleep after surgery.

Morphine not only abolishes REM sleep but induces sleep apnoea in the absence of REM sleep. The 'catching up' period of REM sleep may cause even more profound hypoxaemia after 2–3 days, when morphine administration has ceased.

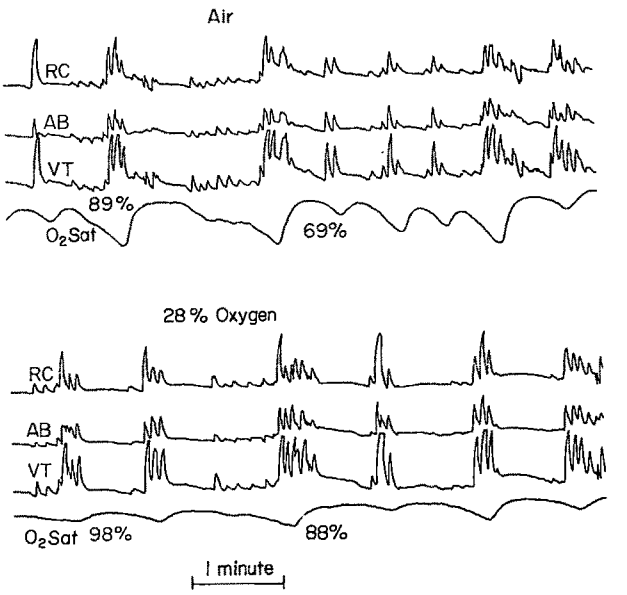

Fig. 5. The breathing pattern of the rib cage (RC), abdomen (AB), tidal volume (VT = RC + AB), and oxygen saturation in a patient breathing either air or 28% oxygen. There are some periods of central apnoea and partial obstruction with paradoxical movement between RC and AB in the air trace.

Effects of sleep on upper airway patency

There is both impairment of rib-cage movement and hypotonia of the upper airway musculature (and thus a tendency to obstructive apnoea) during REM sleep. Some degree of hypotonia occurs also in the diaphragm during REM sleep and during halothane anaesthesia.[33] Thus there is a parallel between the effects of REM sleep and general anaesthesia where phasic and tonic activity of the intercostal and upper airway muscle is grossly impaired but diaphragm function may be mildly compromised.

Obstructive apnoea is caused by closure of the upper airway, which may remain closed despite increased breathing effort.[34] The oropharynx is the only collapsible segment of the upper airway because its walls are too compliant to resist the effects of a negative transmural pressure.[35] Reduced patency is promoted by four factors: negative pressure in the airway lumen, neck flexion, mucosal adhesion once the airway has closed and abnormal anatomy.

A large pressure (as much as 8 kPa) is needed to close the upper airway completely in normal awake man whereas a pressure of < 1 kPa is required during sedation. The large mechanical forces that oppose collapse when awake are due to the tonic and phasic activity induced in the airway muscles by neural mechanisms. This activity dilates the airway, decreases its compliance and increases its resistance to collapse.

It has been shown that in awake subjects all the muscles of the upper airway exhibit phasic activation which just precedes activation of the diaphragm. In this way the upper airway suddenly becomes highly resistant to the collapsing pressure induced in the airway lumen during activation of the rib cage and diaphragm. The phasic activity in the muscles of the upper airway and diaphragm increases *pari passu* during chemical or mechanical loading and a precise balance exists between collapsing and dilating forces in the oropharynx. However, when the neural control of the upper airway is impaired or abolished (as in REM sleep, during anaesthesia or postoperatively during sleep after morphine administration) the phasic activation of the upper airway musculature may either be reduced, become synchronous with, or follow diaphragmatic activation and oropharyngeal closure ensues.[35]

The site of upper airway obstruction

The site of airway obstruction is not known with any certainty. It has long been assumed that the cause of obstruction is hypotonia of the tongue which occludes the oropharynx. Fluoroscopic studies during episodes of sleep apnoea have rarely shown the tongue to be the major cause of obstruction, and a recent review[35] presented persuasive evidence that the soft palate is an important cause of obstructive episodes. However, this may be because of anatomical differences in this structure in some patients with sleep apnoea. Brown *et al.*[36] used an acoustic reflection technique to measure the cross-sectional area of the upper airway and showed an age-related reduction in males. A study of upper airway obstruction in anaesthetised patients suggested that the epiglottis and not the tongue is the major cause of obstruction.

Presentation of data from long term pulse oximetry

The availability of the pulse oximeter for postoperative monitoring presents problems in data management. The conventional method of presenting these data is similar to that shown in Figure 5 where the Spo_2 is plotted together with the pattern of breathing as measured with a Respitrace instrument. This is a useful way of relating the changes in Spo_2 to respiratory pattern, particularly for short periods of data collection. A cumulative plot of Spo_2 for epochs of up to one hour may be a useful way of presenting these data so that the patterns of Spo_2 during long periods of monitoring can be displayed more readily. One form of display[37] is a 'compressed spectral array' in which the oxygen saturation pattern for a whole night can

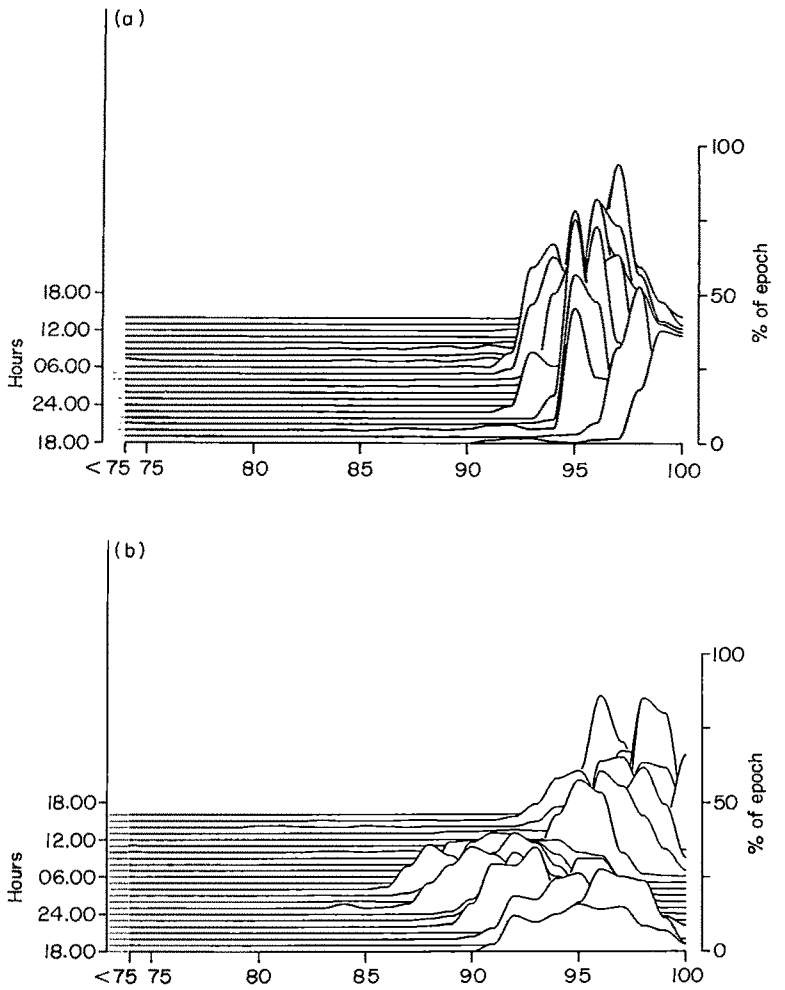

Fig. 6. Continuous monitoring of oxygen saturation (%) displayed for 1-hour epochs after surgery. The effect of 4-hourly intramuscular morphine is shown in panel (a) and the effect of epidural diamorphine in (b).

be shown clearly in a simple diagram (Fig. 6). The percentage of each epoch spent at any Spo_2 is shown and a series of epochs can be plotted for the whole study period.

Figures 6a and 6b illustrate a stable and an unstable pattern of postoperative hypoxaemia. Data are present for 2 hours before and for 18 hours after surgery in a patient who received intramuscular morphine after operation (Fig. 6a). The pattern of oxygen saturation remained reasonably stable through the night with only a small degree of variability from hour to hour. In contrast a second patient who received boluses of diamorphine via an epidural catheter displayed a considerable degree of hypoxaemia, particularly at night, with some degree of recovery when he awoke in the morning but with a tendency to relapse during the following afternoon (Fig. 6b).

This is a useful monitoring system which is suitable for long term data logging and display. It illustrates the severity of postoperative hypoxaemia that can occur in an otherwise normal subject and emphasises the duration of these changes and the association with sleep.

Conclusion

Postoperative hypoxaemia is based on the interaction of two factors: a gas exchange abnormality induced during anaesthesia which may persist for many hours or days into the postoperative period and an abnormality of control of breathing which is manifest by episodic obstructive apnoea rather than a sustained decrease in respiratory rate, and which may last for several days/nights after operation.

Different methods of administering analgesics are likely to cause different degrees of hypoxaemia and it remains to be seen which type is associated with the minimal effect. In the meantime more information is needed on the pattern of postoperative hypoxaemia using a system for automatic data processing similar to that described in this paper.

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Forum

Cytogenetic damage in operation theatre personnel

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Summary

The study in a group of 24 (11 anaesthetists and 13 support staff) was planned to ascertain the cytogenetic risk in a group of theatre personnel who worked in various city hospitals. Their exposure in terms of duration of service vary from 3–30 years. The control group (n = 24) consisted of people with different occupations matched for possible confounding variables. Cytogenetic risk was assessed in terms of chromosome aberration and sister chromatid exchange in 72-hour lymphocyte cultures. A significant increase in the percentage of chromosome aberration was observed. The sister chromatid exchange was double that of the baseline value in 20% of the exposed individuals. These findings indicate the possible risk of cytogenetic damage for staff working in unscavenged rooms.

Key words

Anaesthetic gases; trace concentrations.
Operating rooms; contamination.

Epidemiological studies have presented a controversial picture about the occupational health of anaesthetists. Most of the studies have not indicated mutagenicity on exposure to currently used inhalation anaesthetics.[1] However, the guidelines and standards set forth by The National Institute of Occupational Safety and Health (NIOSH) are not strictly enforced in developing countries, where safety measures at work places are given a lower priority than they deserve. Hence there is a risk of high exposure to waste anaesthetic gases of staff working in unscavenged rooms. Information on the health and the associated genetic risk of theatre staff in India is scarce.

Extensive studies were done in the last decade to ascertain the possible association between operating room work and the outcome of various diseases. The relative risk for reproductive and nonreproductive outcomes were outlined by Buring *et al.*[2] Theatre pollution by waste anaesthetic gases was attributed to be the prime cause for the adverse effects in most of the studies.[3] The concentration of waste anaesthetic gases in theatres is influenced by several factors, such as the type of anaesthetic agent in use, ventilation and type of scavenging system. There is no scavenging to clear the polluted atmosphere in some developing countries. This leads to chronic exposure of theatre staff to waste anaesthetic gases.

Conflicting reports are available on the mutagenic effects of anaesthetic agents. Those anaesthetic agents with a vinyl moiety were found to be mutagenic *in vivo* and *in vitro* systems.[4,5] Short-term, as well as long-term *in vivo* exposure to these agents in anaesthetists, supportive staff and patients did not reveal any increase in chromosome aberration (CA) or sister chromatid exchange (SCE).[1] Information about the health risks of theatre staff and their exposure levels at work are not available in India. The present study therefore aims to monitor biologically the theatre staff who work in an atmosphere without scavenging.

Materials and methods

Blood samples were collected from 24 theatre staff of various city hospitals; 11 were anaesthetists and 13 were theatre assistants. All test subjects examined were clinically healthy; no blood tests were done. One of the anaesthetists is diabetic and is managed on diet. All were exposed to halothane, nitrous oxide and ether either singly or in combination. No other volatile anaesthetics were used. All of the subjects work in theatres of general surgical units or obstetrics and gynaecology units and rotate between these theatres. There are no scavenging systems. No attempt was made to quantify the exposure levels to which the staff were actually exposed. This group was matched with healthy volunteers from various occupations (business, teachers and students).

Information about personal histories and other relevant details were collected from both groups. Peripheral blood lymphocytes of both control and test subjects were cultured[6] for screening of the cytogenetic end points, CA and SCE. Cultures were harvested at 72 hours for both CA and SCE.

Aberrations were classified based on the description of Buckton and Evans[7] as chromatid gap (G′), isochromatid gap (G″) chromatid break (B′) isochromatid break (B″) fragment (F) single minute (M), double minute (DM) dicentric (Dic) polyploidy (Poly) and endoreduplication (End). Preparations for the analysis of SCE were processed according to the method of Kulkarni *et al.*[8] Slides were

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coded and analysed by the same individual. Data were obtained from the analysis of 100 well-spread metaphase plates per sample for CA and 25 well-differentiated second division plates per sample for SCE.

Statistical analysis. Analysis of variance (ANOVA) was used to study the differences between the groups. The original values ($\bar{x}$) were transformed into sin $\bar{x}$ to meet the various criteria for valid application of ANOVA as described in Zar.[9] The formula for transformation is

$$\sqrt{n+0.5}\ \mathrm{Sin}^{-1}\ \sqrt{Y+0.375/n+0.75}$$

where y = number of aberrant metaphase plates
n = number of metaphase plates analysed.

Results

The results are presented in Tables 1–4.

Table 1. Duration of exposure of the theatre personnel.

Serial number	Sample	Sex (M/F)	Smoker/ nonsmoker (S/NS)	Age (years)	Exposure (years)
1	Anaesthetist	M	NS	37	11
2	Anaesthetist	M	NS	45	18
3	Anaesthetist	M	NS	27	3
4	Anaesthetist	M	NS	44	15
5	Anaesthetist	M	NS	53	27
6	Anaesthetist	F	NS	47	19
7	Anaesthetist	F	NS	44	20
8	Anaesthetist	F	NS	39	17
9	Anaesthetist	F	NS	44	18
10	Anaesthetist	F	NS	36	9
11	Anaesthetist	F	NS	38	7
12	Theatre assistant	M	NS	52	28
13	Theatre assistant	M	NS	49	30
14	Theatre assistant	M	NS	36	9
15	Theatre assistant	M	NS	42	23
16	Theatre assistant	M	NS	43	23
17	Theatre assistant	M	NS	36	11
18	Theatre assistant	M	S	32	12
19	Theatre assistant	M	S	33	14
20	Theatre assistant	M	S	34	10
21	Theatre assistant	M	S	32	3
22	Theatre assistant	M	S	33	3
23	Theatre assistant	F	NS	39	3
24	Theatre assistant	F	NS	33	12

Discussion

Mutations contribute significantly to human diseases and congenital malformations, although the extent of this contribution remains unknown. The high level of chromosomal disorders in man emphasises the importance of chromosomal change in human populations.[10]

According to the World Health Organization[11] the most valid approach to assess genetic damage from occupational exposure is by cytogenetic screening. In typical situations of occupational exposure new lesions are inflicted on the DNA of lymphocytes of the individuals which are either unrepaired, repaired or misrepaired. Residual unrepaired and misrepaired lesions appear as chromosomal aberrations. The expected frequency of aberrations would be low unless the exposure is high.

It is evident from the present study that the high incidence of aberrant metaphases (excluding gaps) recorded in the lymphocytes of both anaesthetists and theatre assistants is probably the result of the high exposure to anaesthetic gases (Tables 2 and 3). As seen from the tables, cells with visible chromosome aberrations of unbalanced type such as dicentrics, exchange figures and breaks, are unlikely to survive, whereas those types of aberrations that are balanced (translocations, inversions) are more stable and may not be lethal.[11]

The nitrous oxide (N_2O) concentration increases to a few thousand ppm in unscavenged rooms and operation theatres.[12–14] Hence midwives working in ill-equipped rooms are potentially at risk from high exposure to N_2O pollution.[15] N_2O is not a mutagen itself, but it enhances the mutagenic potential of volatile anaesthetics such as halothane. Halothane in combination with N_2O was found to increase sex-linked recessive lethal mutations in *Drosophila*.[16] A combination of N_2O and volatile anaesthetics is commonly administered to patients and they are present together in the waste anaesthetic gases that are inhaled by operating room personnel. However, in most of the other test systems, halothane was found to be nonmutagenic.[5,17–20]

Anaesthetics with vinyl moiety were found to be positive in both Ames Salmonella bacterial assay[4] and in Chinese hamster ovary (CHO) cells[5] in the presence of rat liver enzymes. Similar observations were recorded in the bone marrow and spermatogonial cells of rats chronically exposed to halothane and N_2O.[21] The increased incidence of chromosomal aberrations was related to the carcinogenic potential of anaesthetic agents.[22]

Table 2. Chromosomal aberrations observed in lymphocytes of anaesthetists.

Serial number	Sex (M/F)	Smoker/ nonsmoker (S/NS)	Age (years) Sample (S)	Age (years) Control (C)	Aberrant metaphases (%) + Gaps S	Aberrant metaphases (%) + Gaps C	Aberrant metaphases (%) − Gaps S	Aberrant metaphases (%) − Gaps C	Aberrations (%) + Gaps S	Aberrations (%) + Gaps C	Aberrations (%) − Gaps S	Aberrations (%) − Gaps C	Types of aberrations (%) Structural G′ S	G′ C	G″ S	G″ C	B′ S	B′ C	B″ S	B″ C	F S	F C	M S	M C	DM S	DM C	Dic S	Dic C	Numerical Poly S	Poly C	End S	End C
1	M	NS	37	37	10	2	5	—	15	2	5	—			10	2													5	—		
2	M	NS	45	44	—	—	—	—	—	—	—	—																				
3	M	NS	27	27	2	—	2	—	2	—	2	—							2	—												
4	M	NS	44	44	22	—	20	—	28	—	20	—	8				10	—			2	—			2	—			4	—	2	—
5	M	NS	53	53	20	—	8	—	26	—	12	—	4		10	—	8	—			2	—							2	—		
6	F	NS	47	48	4	—	4	—	4	—									4	—												
7	F	NS	44	44	8	—	8	—	10	—	10	—					2	—					6	—					2	—		
8	F	NS	39	39	6	—	4	—	12	—	6	—			6	—							6	—								
9	F	NS	44	42	12	—	6	—	14	—	6	—	8				2												2	—	2	—
10	F	NS	36	36	14	—	14	—	28	—	22	—	4		2	—	12	—	2	—			4	—			4	—				
11	F	NS	38	39	6	—	4	—	6	—	4	—	2														2	—	2	—		

For abbreviations of aberrations please see text.

Table 3. Chromosomal aberrations observed in lymphocytes of theatre assistants.

Serial number	Sex (M/F)	Smoker/ nonsmoker (S/NS)	Age (years) Sample (S)	Age (years) Control (C)	Aberrant metaphases (%) + Gaps S	Aberrant metaphases (%) + Gaps C	Aberrant metaphases (%) − Gaps S	Aberrant metaphases (%) − Gaps C	Aberrations (%) + Gaps S	Aberrations (%) + Gaps C	Aberrations (%) − Gaps S	Aberrations (%) − Gaps C	Types of aberrations (%) Structural G′ S	G′ C	G″ S	G″ C	B′ S	B′ C	B″ S	B″ C	F S	F C	M S	M C	DM S	DM C	Dic S	Dic C	Numerical Poly S	Poly C	End S	End C
1	M	NS	52	53	18	—	8	—	28	—	8	—	12	—	8	—	4	—	2	—									2	—		
2	M	NS	49	48	14	2	4	2	14	2	4	2	10	—					2	—											2	2
3	M	NS	36	37	4	2	6	—	10	2	8	—	2	—	—	2					4	—					2	—	2	—		
4	M	NS	42	41	10	—	6	—	10	—	6	—			4	—	2	—	2	—							2	—				
5	M	NS	43	41	10	—	8	—	12	—	10	—			2	—	8	—					2	—								
6	M	NS	36	37	24	—	18	—	28	2	22	—	6	—	—	2			4	—			4	—	2	—					6	—
7	M	S	32	30	10	—	10	—	16	—	16	—					12	—			4	—										
8	M	S	33	32	18	—	2	—	22	—	2	—	10	—							2	—										
9	M	S	34	35	26	2	4	—	40	2	6	—	10	—	24	2	6	—														
10	M	S	32	30	26	—	14	—	32	—	14	—	4	—	14	—	2	—	10	—									2	—		
11	M	S	33	32	8	—	2	—	10	—	2	—			8	—			2	—												
12	F	NS	39	39	10	—	6	—	10	—	6	—			4	—							2	—					4	—		
13	F	NS	33	32	16	—	10	—	16	—	10	—			6	—											6	—	4	—		

For abbreviations of aberrations see text.

Summary of the ANOVA for Tables 2 and 3.

	Sum of squares (SS)	Degrees of freedom (DF)	Mean square (MS)	F
Total	351 113.07	47		
Between groups	83 569.46	2	41 784.73	7.028*
Error	267 543.61	45	5945.41	

*Significant at 5% level.

Surprisingly, we found only chromatid gaps and an isolated incidence of endoreduplication in the control group. Gaps do not represent true discontinuity in DNA so they were not considered for statistical analysis.[11] The frequencies of chromosomal aberrations encountered in control populations from the literature indicates that exchange-type aberrations vary between 7 and 12 in 10 000 metaphases, with an average of 7.6 exchange events in 10^4 cells. The frequency of breaks is much higher and varies from 14 to 100×10^{-4} cells.[23] Our analysis of chromosome aberrations represents data obtained from 100 metaphases/individual, so this is probably why it was not possible to detect the reported low baseline frequency of other types of aberrations in the control population.

The mean frequency of SCE was doubled in 20% of the exposed individuals. Such an increase was demonstrated earlier in anaesthetists exposed to vinyl agents.[5] However, SCE tests in different groups of hospital personnel has not

Table 4. Frequency of SCEs observed in lymphocytes of control and theatre personnel.

Slide number	Sex	Age Sample	Age Control	Smoker/ nonsmoker (S/NS)	Mean X S	Mean X C	SCE standard deviation S	SCE standard deviation C	Range S	Range C
1	M	37	37	NS	3.1	3.76	1.71	0.83	1–7	3–6
2	M	45	44	NS	7.08	6.36	4.396	1.89	1–18	4–11
3	M	27	27	NS	7.84	3.76	2.426	1.535	3–14	3–8
4	M	44	44	NS	9.44	6.36	4.68	1.89	2–20	4–11
5	M	53	53	NS	7.72	8.2	2.04	2.10	4–11	5–12
6	M	52	53	NS	5.48	8.2	2.04	2.10	2–10	5–12
7	M	49	48	NS	4.8	5.48	1.75	2.78	2–8	2–12
8	M	36	37	NS	3.72	3.76	1.137	0.83	2–6	3–6
9	M	42	41	NS	3.8	3.6	1.04	1.60	2–6	2–8
10	M	43	41	NS	5.36	3.6	1.468	1.60	2–6	2–8
11	M	36	37	NS	7.8	3.76	2.327	0.83	5–14	3–6
12	M	32	30	S	12.24	4.48	5.08	2.36	6–25	2–10
13	M	33	32	S	5.56	7.72	1.556	1.72	3–9	4–11
14	M	34	35	S	5.28	3.36	1.208	1.22	3–8	2–6
15	M	32	30	S	4.8	4.48	2.48	2.36	2–15	2–10
16	M	33	32	S	5.0	7.72	0.957	1.72	3–7	4–11
17	F	47	48	NS	7.4	3.76	4.1	1.05	2–16	2–6
18	F	44	44	NS	4.4	7.88	2.75	3.07	1–11	2–12
19	F	39	39	NS	4.48	6.28	2.85	2.894	1–3	2–13
20	F	44	42	NS	6.66	7.32	4.53	1.6	1–18	5–11
21	F	36	36	NS	7.44	2.44	4.35	1.78	2–21	5–12
22	F	38	39	NS	9.04	6.28	1.567	2.89	6–11	2–13
23	F	39	39	NS	5.4	6.28	1.84	2.89	3–10	2–13
24	F	33	32	NS	6.12	4.96	2.63	2.58	3–16	2–12

indicated any mutagenic effect as a result of occupational exposure to waste anaesthetic gases.[1]

Analysis and interpretation of occupational hazards can be complicated by several factors. These include the type of anaesthetic equipment, the anaesthetic agent, exposure time, health status, familial differences and above all efficiency of any scavenging system. Moreover, individual responses to the same chemical and to the same dose may vary considerably.

Pollution in the operation theatres could be the cause of these changes. There are reports which highlight the importance of scavenging systems in minimising pollution and the associated adverse effects.[13,15,24] These methods should be implemented to ensure safe exposure levels to minimise the risks to health of exposed individuals.

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Prevention of TUR syndrome by detection of trace ethanol in the expired breath

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Summary

Previous studies suggest that severe symptoms of the 'TUR syndrome' occur from transurethral prostatic resection only when the volume of irrigant absorbed exceeds 2000 ml. An ethanol-containing irrigating fluid was used in this study of 100 transurethral resections so that the irrigant absorption could be monitored by measuring ethanol in expired air. Fluid absorption was found in 41 patients, and in nine of them the volume of irrigant absorbed exceeded 1000 ml. Four of these operations were terminated promptly when the ethanol monitoring indicated rapid massive absorption that threatened to exceed 2000 ml. There were few and only mild adverse effects of the irrigant by following this regimen. It is concluded that ethanol monitoring makes it possible to prevent the TUR syndrome by selective termination of those operations in which large amounts of irrigant is absorbed.

Key words

Complications; glycine.
Surgery; prostate.

Absorption of the irrigating solution used during transurethral prostatic resection (TUR) is the accepted cause of the 'TUR syndrome'. The symptoms include hypertension, visual disturbances, dyspnoea, mental changes and circulatory shock.[6] The severity of the TUR syndrome depends on the volume of irrigant absorbed. Mild symptoms occasionally occur from absorption of 1000 ml of irrigant[6-9] and in most patients when the 'leakage' of fluid reaches 2000 ml, whereas with greater absorption volumes symptoms become more frequent and more severe.[6,7,9] To avoid the TUR syndrome it would therefore be necessary to detect fluid absorption that exceeds 2000 ml.

The present study examines prompt termination of TUR when the volume of irrigant absorbed exceeds 2000 ml, as a means of preventing the severe symptoms of fluid absorption. This approach requires immediate detection of all fluid absorption during prostatectomy. An irrigating fluid containing tracer amounts of ethanol was used for this purpose. This permitted fluid absorption to be indicated at any time during TUR by measuring the concentration of ethanol in the patient's exhaled breath.[8-11]

Materials and methods

One hundred patients between the ages 54 and 91 years (mean, 71; SD, 7) who underwent transurethral prostatic resection (TUR) in epidural analgesia were studied. Patients in whom only a transurethral incision of the prostate was performed were excluded, as well as those who received general anaesthesia. The series was consecutive with these exceptions. The weight of the resected prostatic tissue ranged from 9 to 124 g.

Oxazepam 25–50 mg was given orally as premedication. Epidural analgesia was induced with 9–14 ml 2% mepivacaine with adrenaline (Carbocain-adrenalin; Astra, Södertälje, Sweden). The intravenous fluid supplementation consisted of 1500–2000 ml Ringer's acetate solution (sodium content 130 mmol/litre, potassium 4 mmol/litre). Five hundred millilitres of dextran 70 in normal saline (Macrodex; Kabi, Stockholm, Sweden) was also administered in 21 patients where the blood loss exceeded about 700 ml. Red cell concentrate was transfused in 13 operations and blood loss was measured by means of the HemoCue system (Leo Diagnostics, Helsingborg, Sweden).

The irrigating fluid used during resection was water-containing 1.5% glycine and 1% ethanol (v/w) (osmolality 400 mosmol/litre; Baxter, Stockholm, Sweden). Saline 0.9% was used after operation. Bladder irrigation was performed using an intermittent technique. Every 10 minutes during all operations, and every 5 minutes whenever irrigant absorption was detected, the end-expiratory ethanol concentration (EB-ethanol) was measured with an Alcolmeter S-D2 (Lions Ltd., Barry, Wales). The patient was instructed to take a deep breath and then to breathe into the mouthpiece of the Alcolmeter. The values so obtained represented the corresponding blood ethanol concentration, in steps of 0.05 mg/ml (1 mg/ml = 21.7 mmol/litre).[9-11] The volume of irrigant absorbed was estimated from the ethanol concentration in the expired breath (EB-ethanol) at the end of the resection and the time factor (i.e. the time period during which ethanol was detected in the expired breath) according to the formula:

Absorption (ml) = 3063 EB-ethanol (mg/ml) + 21.5 time (minutes) − 313.

This formula is based on comparisons between ethanol readings and incremental measurements of the volumetric fluid balance corrected for blood loss in the course of 60 transurethral resections.[9]

The patients were divided into four groups for the presentation of results, depending on whether fluid absorption was not detectable (< 100 ml), small (100–499 ml), moderate (500–999 ml) or large (> 1000 ml).

Results

Fluid absorption was detected in 41 patients, and in nine the volume of irrigant absorbed exceeded 1000 ml (Table 1). There were no significant differences in age or resection time between patients with various degrees of irrigant absorption (analysis of variance, $p > 0.05$; Table 1); however, resections with a large irrigant absorption had a significantly greater blood loss as compared to the other operations (Mann–Whitney's test, $p = 0.04$) (Table 1). The patients with the largest blood losses in the case series, on the other hand, usually had only moderate irrigant absorption (Fig. 1); this is in accordance with previous studies.[12,13] No patient with nondetectable or small irrigant absorption (i.e. up to 499 ml) had any symptom of the TUR syndrome. There were increases in systolic blood pressure of 10–20 mmHg that were related to the absorption in three out of nine patients with fluid absorption of a moderate degree (500–999 ml). The following patient (aged 66 years and in good health) experienced mild symptoms.

Case 1. The patient experienced transient burning and prickling sensations in both hands when ethanol was first detected in the expired breath (Fig. 2). However, since the

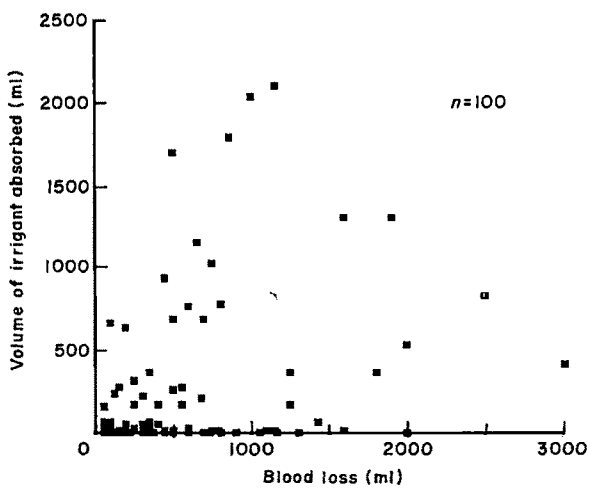

Fig. 1. The total volume of irrigant absorbed compared with the blood loss in all patients who had transurethral resection of the prostate.

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Table 1. Patient age and operative data in 100 transurethral prostatic resections divided into four groups according to the degree of irrigant absorption.

	Absorption volume (ml)			
	Nondetectable	100–499	500–999	>1000
Patients (number)	59	23	9	9
Age; years, mean (SD)	71 (7)	72 (7)	66 (7)	72 (6)
Resection time; minutes, mean (SD)	48 (24)	54 (25)	63 (18)	63 (20)
Blood loss; ml, median and (range)	310 (25–2000)	350 (50–3020)	600 (80–2500)	930 (490–1900)
Fluid absorption; ml, mean (SD)		210 (102)	725 (120)	1545 (385)

Table 2. Operative data in five patients with intravascular irrigant absorption who developed one or several symptoms of the TUR syndrome. Routine blood chemistry[6] was made on admission to the hospital, and repeated about 30 minutes after prostatectomy (except where indicated).

	B-Hb (g/litre)	S-Na (mmol/litre)	S-K (mmol/litre)	Prostate weight (g)	Fluid absorbed (ml)	Blood loss (ml)
Case 1						
Before TUR	154	137	4.7			
After TUR	136	134	5.3	36	965	450
Case 2						
Before TUR	148	136	4.2			
After TUR	127	125	4.3	50	1435	550
Case 3						
Before TUR	113	138	4.4			
After TUR	104*	130*	4.0	15	1800	860
Case 4						
Before TUR	154	139	3.9			
After TUR	110	126	5.1	62	2045	1000
Case 5						
Before TUR	142	139	3.9			
After TUR	119*	129*	haemolysis	78	2110	1150

*Blood sample drawn 1 hour after the operation.

absorption was of only moderate degree, surgery was not interrupted, and the operation lasted an additional 30 minutes (Fig. 2). The patient reported exhaustion and slight nausea from 30 minutes after the operation, but he did not vomit (Table 2).

Five out of nine patients with a large irrigant absorption (> 1000 ml) displayed elevation of systolic blood pressure of 20–40 mmHg. Four of the operations were stopped when the ethanol monitoring indicated rapid fluid absorption that threatened to exceed 2000 ml. The courses of these resections are described below. Operative data and ethanol readings are shown in Table 2 and in Figure 2, respectively. All of these patients were previously healthy with the exception of Case 2, who suffered from asthma and received long-term medication with terbutaline and theophylline.

Case 2. After 40 minutes of TUR, the patient (aged 72 years) complained of prickling skin sensations while the ethanol monitor indicated that irrigant was being absorbed at a very rapid rate. The surgeon was informed and stopped the operation. The patient reported slightly blurred vision when the bladder catheter was inserted. He was moderately hypotensive (systolic pressure 80–85 mmHg) in the recovery room.

Case 3. Rapid absorption was detected after 5 minutes of TUR. The patient (aged 60 years) declared that his head was under 'pressure', and showed marked flushing. The surgeon tried to control absorption by using a lower fluid

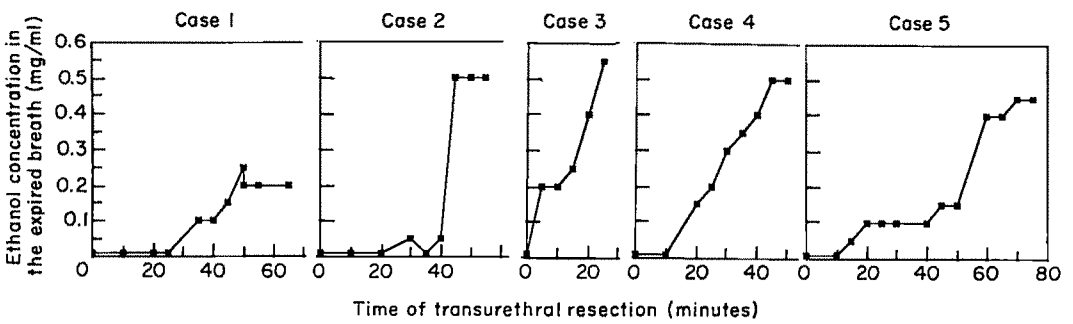

Fig. 2. The ethanol concentration in the patient's expired breath in the course of five operations where intravascular irrigant absorption gave rise to mild symptoms of the TUR syndrome. The irrigating fluid contained 1.5% glycine and 1% ethanol.

pressure. This was not successful, however, and when the absorption rate increased dramatically 15 minutes later, the TUR was stopped immediately. The patient was tired, slightly hypotensive (systolic pressure 80–100 mmHg) and had repeated diarrhoea after the operation.

Case 4. The urologist tried to stop absorption in this patient (aged 66 years) when ethanol was detected in the expired breath (Fig. 2) by using a lower fluid pressure. The absorption increased, however, and 30 minutes later the urologist was urged to stop the resection. The patient's systolic blood pressure increased from 110 to 150 mmHg during the last 15 minutes of the operation. He reported slight nausea after the operation, but did not vomit.

Case 5. Low-grade irrigant absorption was detected after 10 minutes of the TUR in this patient (aged 69 years). Fifty minutes later the rate of fluid absorption increased dramatically. The urologist was informed and chose to stop the resection at once. The systolic pressure increased from 90 to 130 mmHg at the end of the rapid absorption. The patient was markedly pale, but felt well.

One patient's large irrigant absorption had leaked into the perivesical space.

Case 6. The patient (aged 77 years) complained of slight abdominal discomfort after 40 minutes of TUR. Ten minutes later there was sudden bradycardia and hypotension, which was treated with incremental intravenous doses of ephedrine. The EB-ethanol level increased from 0.00 to 0.20 mg/ml, which persisted after the operation, and perivesical absorption was suspected. A *sectio alta* was performed without delay, and 1700 ml of irrigating fluid was drained from the perivesical space.

Discussion

Ethanol indication is a simple and practical method for screening irrigant absorption in patients who have transurethal prostatectomy. The expired-breath test provides essentially the same information as serial determinations of the serum sodium level, and correlates well with incremental volumetric measurements of the irrigant absorption corrected for time.[9–11] Alcohol intoxication has not been observed with the irrigant solution containing 1% ethanol, which was registered for routine use in Sweden in 1989.[9] It is still unclear, however, what safety measures should be undertaken by the operating team when fluid absorption is detected. It is necessary to determine what is 'safe' fluid absorption in this context. It has been demonstrated by careful volumetric measurements[13] and by marking the irrigant with radioisotopes[14] that some irrigating fluid is absorbed by the patient in almost every TUR performed. Symptoms of fluid absorption, on the other hand, occur in less than 10% of resections.[1–4,7,9] The discrepancy in incidence between fluid absorption and symptoms can probably be explained by a requirement for a large fluid volume to be absorbed before adverse effects ensue. This implies the existence of a 'safe' level of fluid absorption, where irrigant can enter the body without causing severe sequelae.

The smallest volume of irrigant absorbed known to give rise to symptoms is about 1000 ml,[6–9] a fact that is further supported by the present study (Table 2). Naturally, if it is considered that any adverse effect of the irrigating fluid is unacceptable, resections must be terminated just before this volume has been absorbed (i.e. at about 0.30 mg/ml of ethanol in the expired breath). However, in previous studies only very mild and transient symptoms arose in some patients from the absorption of between 1000 and 2000 ml of the irrigant containing 2.2% glycine[6] and 1.5% glycine +1% ethanol.[9] This suggests that it is probably appropriate to use a limit for 'safe' absorption that is greater than 1000 ml, otherwise, operations will be disturbed or interrupted when there is no real danger of serious sequelae.

Resections were stopped in the present study when up to about 2000 ml of irrigant had been absorbed. There were only few and very mild symptoms of fluid absorption with this regimen, and no TUR syndrome occurred. On the other hand, in previous studies moderate to severe symptoms of this syndrome developed in four out of four patients[6] and in four out of five patients[9] where the fluid absorption exceeded 2000 ml. Furthermore, Norris and co-workers[1] have described five patients who developed severe forms of the TUR syndrome during prostatectomy, which led to early postoperative death in two. The volume of irrigant absorbed, as estimated from dilution of serum sodium, was greater than 2400 ml in all cases. The dilution of serum electrolytes indicated a fluid absorption of between 3000 and 4000 ml in a TUR syndrome with fatal outcome reported by Aasheim.[2] Henderson and Middleton[3] described 14 patients who developed the TUR syndrome. It was estimated that 12 of these patients had absorbed more than 2300 ml of irrigating fluid. Alexander and co-workers[5] found that 3000 ml of irrigant could not be accounted for during an operation where the patient developed hyponatraemic cardiovascular collapse. It seems, therefore, to be relatively safe to allow irrigant absorption up to a volume of 2000 ml during a resection operation, while larger absorption volumes are dangerous and should be prevented.

Some of the mild symptoms of fluid absorption observed in this study deserve a comment. Prickling and burning sensations in the skin of the hands and face (Cases 1 and 2) appears to be a common early sign of rapid massive absorption of irrigant that contains glycine; it is of an unpleasant character, but subsides within 2 minutes even if irrigant absorption continues.[8] Nausea (Cases 1 and 4) typically begins 30 minutes to 1 hour after completion of a resection and persists for 1–3 hours. However, after absorption of only between 1000 and 2000 ml of irrigant the nausea is mild and does not lead to vomiting.[6–9] Diarrhoea is a rare sign of fluid absorption (Case 3), which we have seen in only a few patients who developed severe forms of the TUR syndrome.[15] Watery diarrhoea appears at the end of the resection and recurs several times during 1–2 hours. The mechanism is obscure, but it is possible that irrigant water acts as an enema by diffusing through the intestinal capillaries to accumulate in the lumen of the bowel. A similar kind of diffusion occurs to the pleural and peritoneal cavities in patients who develop the TUR syndrome.[1]

There was only one patient in the present series with marked perivesical accumulation of irrigating fluid (Case 6). Such absorption may occur from open perforations of the prostatic capsule. There is no doubt that the expired-breath test detects perivesical absorption less readily than intravascular absorption. However, in contrast to the often-quoted results of Oester and Madsen,[14] several studies of transurethral resections performed in this hospital have revealed only a few occasional patients with major perivesical irrigant extravasation.[9–13] The exhaled ethanol concentration decreases within 5 minutes after bladder irrigation is stopped with the commoner intravascular absorption. On the other hand, the ethanol level is unchanged after perivesical irrigant leak, or is increased after completion of the TUR.[9–11] This pattern was seen in Case 6, and the ethanol monitoring aided greatly the early diagnosis in this patient.

In conclusion, ethanol monitoring allows the operating team to control irrigant absorption. Severe adverse effects of the irrigant can be prevented by prompt termination of operations in which rapid massive absorption occurs, before an absorption of 2000 ml is detected.

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Incidence and range of carboxyhaemoglobin in blood for transfusion

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Summary

No statistically significant difference was found between the levels of carboxyhaemoglobin detected in samples from 42 blood units and their sample side arms. A cooximeter was used. However, carboxyhaemoglobin in a range of 1.1–6.9% was found in 18 out of a further 100 side arm samples taken randomly from the blood bank.

Key words

Blood; carboxyhaemoglobin
Transfusion.

Carboxyhaemoglobin (COHb) increases of more than 3% were reported previously in two patients after transfusion of six or more units of blood,[1] and were the result of the presence of COHb in several of the units given to each patient. We used a cooximeter to analyse samples taken from 166 donor units to ascertain the incidence and range of COHb in stored blood.

Method

Samples of 1–1.5 ml blood were carefully aspirated from 51 used donor units, and their sample side arms, through wide bore needles, into 2-ml syringes. Each sample was carefully agitated before analysis on the intensive therapy unit by a Corning 2500 Cooximeter. This instrument takes 0.2 ml of anticoagulated whole blood, haemolyses it with ultrasound, then measures absorbances at seven specific wavelengths of light. It calculates total haemoglobin concentration (g/dlitre) from this and the percentage levels of the haemoglobin derivatives oxyhaemoglobin, reduced haemoglobin, methaemoglobin, and COHb. The manufacturer claims accuracy of 1 SD over the range 0–100% for COHb estimation provided that total haemoglobin measured is in the range 8–22 g/dlitre, that the haemoglobin derivatives

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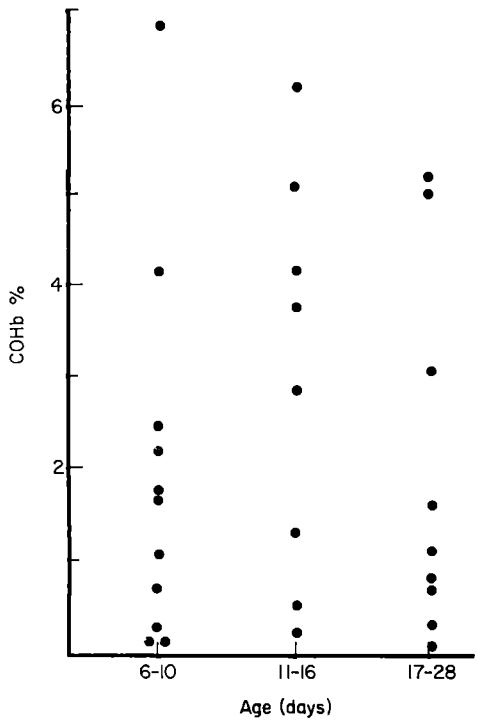

Fig. 1. Measurements from 25 sample side arms positive for carboxyhaemoglobin from 100 randomly tested.

add up to 100% (1 SD%), and that no single derivative was given a negative value.[2] One single sample with COHb present was tested 10 times to assess the variability of this cooximeter. Statistical analysis of results was performed using Student's *t*-test.

No statistical difference was detected between COHb levels in donor units and their sample side arms. We therefore went on to collect blood from 6-cm lengths of 115 sample side arms taken randomly from the blood bank over the course of a month. All these samples were analysed within 2 hours of collection by the method described above.

Results

A single sample tested 10 times had a mean COHb value of 3.37%; the coefficient of variation was 1.4% (three at 3.3% and seven at 3.4%). The results from nine donor units/sample side arms were rejected because they did not meet the cooximeter accuracy criteria. Measurements from the 12 donor units and sample side arms in which COHb was detected showed a mean COHb of 3.7% (SD 2.1%) and 3.6% (SD 2.0%) respectively. There is no statistically significant difference between the groups.

The results from 15 blood bank sample side arms were rejected because they did not meet the cooximeter accuracy criteria. The measurements from the 28% of blood bank sample side arms in which COHb was present are shown in Figure 1. COHb at levels greater than 1% was present in 18 out of 100 sample side arms; median COHb 3.0%, range 1.1–6.9%.

Discussion

COHb is one of the products of haemoglobin metabolism, and may be found at a concentration of up to 0.7% in those not exposed to carbon monoxide.[2] Environmental carbon monoxide pollution may raise COHb levels up to 2% in nonsmokers, although there is evidence that this influence is declining.[3] The highest COHb levels reported in the general public occur in smokers, who may have levels up to 10.6%. Severe haemolytic states may also produce COHb levels of up to 6%.

Millar and Gregory in 1972, demonstrated that the level of COHb in donated blood remains virtually unchanged during and beyond its normal storage life.[4] The units we found with raised COHb levels were thus almost certainly donated by smokers, and the COHb was preserved by the storage conditions.

Our results indicate that approximately one in five donor units contain COHb levels greater than 1%, and we have previously reported cases in which COHb levels have reached more than 3%.[1] The clinical significance of COHb at levels of less than 5% is unknown. Tissue hypoxia is known to be the main effect of low levels of COHb produced by carbon monoxide inhalation;[5] the oxygen-carrying capacity of the blood is reduced by the presence of COHb and carbon monoxide shifts the oxyhaemoglobin curve to the left, by effects on 2,3-DPG, so decreasing the tension at which oxyhaemoglobin dissociates. A COHb level of 5% produces the same degree of tissue hypoxia as breathing air at 8000–10 000 feet altitude. Normal adults at rest respond to these levels of COHb by increasing oxygen extraction from the blood.[6] This is in contrast to hypoxic hypoxia where cardiac output and ventilation rate are increased. Increases in oxygen extraction are compensated for by increased coronary blood flow in the normal heart, and an insignificant decrease in coronary sinus oxygen tension occurs.[7,8] Similar measurements in adults with ischaemic heart disease show that coronary blood flow cannot be increased, which results in significant decreases in coronary sinus oxygen tension.[7,8] Treadmill testing of patients with stable angina in whom a COHb level of 5% was produced by 4 hours' exposure to carbon monoxide demonstrated a shortened time to onset of angina and increased pain.[9] Ischaemic changes on ECG occurred earlier and lasted longer than when exercise was conducted in the presence of carbon monoxide.[9] COHb levels of 5–9% also increase the tendency to intermittent claudication in patients with peripheral vascular disease, and decrease exercise tolerance in those with lung disease.[10,11] A tendency to arrhythmias, decreased visual acuity, and effects on mental function have also been observed in normal adults at these levels.[5] This evidence has led Turino to state that the safest level of carbon monoxide exposure for the general public is the lowest that can be achieved.[5]

Infusion of blood containing COHb may have significant effects in patients with ischaemic heart disease and in the critically ill, and consideration should be given to minimising the use of blood contaminated with COHb in such patients. Methods suggested for reducing the level of COHb in blood for transfusion have included asking donors to refrain from smoking, giving them oxygen therapy, and asking them to exercise before donation.[12] These measures have never been employed because of the reduction in blood donation that would almost certainly result.

We have shown that donor units containing COHb can be identified by using a cooximeter to analyse blood taken from a 6-cm length of side arm. Donor units can be screened when a patient is judged to be at risk, and those units that contain COHb returned intact to the blood bank for use in less critical patients. We suggest that hospitals already in possession of a cooximeter should start this practice, but the number of patients likely to be at risk from COHb in blood for transfusion is so small that purchase and maintenance of a cooximeter for donor unit screening alone is probably not justified. We cannot be sure, however, until further investigation of the effect of

COHb infused into the critically ill at blood transfusion is performed.

Acknowledgments

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Pre-operative anxiety and serum potassium

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Summary

Small decreases in serum potassium in a study of 200 pre-operative patients were demonstrated in those who had an increase in anxiety, as measured on a linear analogue anxiety scale, in the 24 hours before anaesthesia. The possible aetiology and implications of this change are discussed. The combination of temazepam and a pre-operative visit by the anaesthetist effectively reduced pre-anaesthetic anxiety in 60% of patients.

Key words

Ions; potassium.
Anxiety.

The presence of anxiety is almost universal in the pre-operative patient, and has many aetiological factors.[1] To the patient it is an unpleasant state of uneasiness or tension caused by apprehension of possible future misfortune, while to the anaesthetist it is associated with altered pharmacokinetics of anaesthetic agents, with increases in post-operative narcotic requirements and even with prolongation of hospital stay.[2]

Pre-operative anxiety is known to cause an increase in plasma adrenaline levels of 40% even in patients who have received anxiolytic premedication, and significant correlation exists between changes in anxiety as measured using a linear analogue anxiety score and changes in plasma adrenaline concentrations.[3] Adrenaline causes an increased uptake of potassium into the cells via the beta-adrenoceptor modulated Na^+/K^+ ATPase system.[4,5] Exogenous adrenaline infusion[6,7] and dopamine, dobutamine[8] and salbutamol[9] all cause a decrease in serum potassium in keeping with activation of this system, and beta-adrenoceptor blockers attenuate this decrease in serum potassium.[10]

The aim of this study was to examine the relationship

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Table 1. Demographic details.

	n	Age, years (SD)
Male	83	45.9 (18.5)
Female	117	38.9 (16.2)
Both	200	41.8 (17.5)

between the change in anxiety experienced by the pre-operative patient and any subsequent alterations in the concentrations of serum potassium.

Method

Two hundred patients, aged 16 to 75 years, admitted for elective surgical procedures were studied. Informed consent for participation in the study was obtained, together with Regional Ethics Committee approval. Patients scheduled to receive bowel preparation,[11] those receiving beta-adrenoceptor agonist or antagonists, diuretics, insulin, potassium replacement therapy or intravenous fluids were not studied because these may all affect serum potassium concentrations.

Patients were asked, on the afternoon before surgery, to score their anxiety on a standard visual analogue anxiety scale, with extremities labelled 'not anxious' and 'as anxious as you can possibly imagine.' A sample of venous blood was then taken from the antecubital fossa through a 21-gauge needle for the routine pre-operative blood tests; 6 ml of this sample was placed in a plain glass container for subsequent potassium estimation. Premedication was with oral temazepam 1.5 hours before operation in a dose of 10 mg for those under 60 kg, 20 mg for those who weighed 61–90 kg and 30 mg if over 90 kg.

Patients were asked to score their anxiety again, immediately on arrival at the anaesthetic room, using the linear analogue anxiety scale. A further 6-ml of venous blood was obtained for potassium estimation through a cannula which was subsequently used for the administration of anaesthetic drugs.

Those blood samples not immediately analysed were centrifuged and stored at 4°C. The absence of haemolysis before analysis was ensured by visual inspection by an independent laboratory technician and those samples that showed haemolysis were excluded from the study. Potassium concentrations were determined using a Beckmann Astra 8 channel analyser. Changes in excess of 0.1 mmol/litre were considered significant based on precision of routine quality control.

Statistical analysis was performed using paired Student's *t*-test for potassium concentrations, Wilcoxon rank sum test for linear analogue anxiety scale results and correlation coefficient. $p < 0.05$ was used as an index of statistical significance.

Results

Studies were carried out in 202 patients; two were withdrawn because of haemolysis of one of the blood samples. Demographic details are shown in Table 1. No patient refused to participate in the study. They all completed the linear analogue anxiety scales correctly. Five patients (three male, two female) on the day before surgery claimed to have no anxiety, while four (one male, three female) claimed to have maximum anxiety. Four patients (two male, two female) immediately before anaesthesia, claimed to have no anxiety, while four (one male, three female) claimed to have maximum anxiety.

The mean change in anxiety score was +0.5 cm (male +0.3, female +0.7 cm). This change was not statistically significant. Mean change in potassium was −0.03 mmol/litre (male −0.05, female −0.02 mmol/litre) and again was statistically insignificant (Table 2).

Thirteen patients had no change in anxiety, 67 an increase, and 120 (60%) had a decrease. Of the patients who had an increase in anxiety (33%), potassium decreased by a mean of 0.13 mmol/litre, which was of borderline statistical significance ($p = 0.05$, paired *t*-test). Change in anxiety, as measured by the visual analogue scale was related to change in potassium (ΔK^+) by the equation:

Change in analogue score $= 0.49 - 1.25 \times \Delta K^+$ ($p < 0.05$), which indicates that a small decrease in potassium occurs with increasing anxiety.

Discussion

The results of this study demonstrate that there is a relationship between changes in anxiety and changes in serum potassium, although the potassium change is of modest proportions. It is already established that endogenous adrenaline levels change when anxiety changes, even in the patient who has received a premedicant drug.[3] It is probable that the potassium changes in this study were caused by alterations in the amount of endogenous adrenaline secreted by the patient, since a significant correlation exists between anxiety and adrenaline levels. The relationship between increased anxiety levels and increased adrenaline levels was used to explain the hypokalaemia associated with multiple trauma,[12] and the occasional finding of unexpected hypokalaemia in the healthy patient admitted to hospital for routine surgery.[13]

The other significant finding in this study was that 60% of patients who received a temazepam premedication at the dose detailed in the method, and who had a pre-operative visit by an anaesthetist, had less anxiety immediately before induction when compared with one day previously. It is possible that there would have been larger changes in serum potassium had there been significant changes in anxiety, but it was considered to be unethical to withhold premedication or a pre-operative visit by an anaesthetist in so many patients.

Adrenaline levels increase by 40% in the patient who has received premedication. This is a relatively modest increase when compared with increases of 15-fold and more demonstrated in patients immediately after myocardial infarction,[14,15] and this large increase in adrenaline may well contribute to the arrhythmias seen in these patients. The

Table 2. Changes in potassium and anxiety.

	Males (83)	Females (117)	Both (200)
Change in linear analogue anxiety scale in cm (SD)	0.26 (2.26)	0.66 (4.39)	0.53 (3.69)
95% confidence limits	0.49	0.80	0.51
Change in serum potassium in mmol/litre (SD)	−0.04 (0.46)	−0.02 (0.46)	−0.03 (0.46)
95% confidence limits	0.09	0.08	0.06

implication for the extremely anxious pre-operative patient is that potassium changes may occur which may encourage arrhythmias in the peri-induction phase of anaesthesia, and may exacerbate hypotension after induction as a result of relative hypokalaemia.[16] If this is the case, adequate premedication with anxiolytic, and possibly beta-adrenoceptor antagonist drugs would block this response both at a cortico-adrenal level and also at the Na^+/K^+ ATPase receptor where the adrenaline encourages intracellular migration of the potassium.

In conclusion, the combination of adequate doses of temazepam and a pre-operative visit by an anaesthetist are an effective pre-operative anxiolytic, and increases in anxiety are associated with small decreases in potassium.

Acknowledgments

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A difficult tracheal intubation as a result of obesity and absence of teeth

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People who are overweight are frequently told they are putting their health at risk, but few realise that they pose greater problems as patients undergoing anaesthesia and surgery.

A 31-year-old obese woman who weighed about 89 kg was suffering from gynaecological problems in 1984. She was admitted to a hospital in Northern Ireland for a routine oophorectomy which was performed on the afternoon of 15 June. Unfortunately, after anaesthetic complications at induction of anaesthesia, she had to be transferred to the intensive therapy unit (ITU) of another hospital where she remained for a month, at times seriously and even critically ill, although she eventually made a good recovery. Subsequent investigations revealed that the patient had suffered from acid aspiration syndrome which had damaged her lungs. She sued unsuccessfully in negligence.

The background facts

Lord Justice MacDermott said that it was not disputed that Dr O, who was a registrar in anaesthetics on a short-term attachment to the hospital, was experienced and competent (he obtained his Irish and English Fellowships in 1983 and 1984) and capable of anaesthetising the plaintiff alone and unsupervised. There was a risk in any operation of regurgitation and aspiration of stomach fluid which was acidic and it was well known that any such aspiration into the patient's airways could cause damage. The risk was a factor which had to be borne in mind by all practising anaesthetists; it could be increased by either or both of two matters: a patient's obesity and the absence of teeth. The plaintiff was missing three central teeth in the upper jaw; such a gap could make it more difficult to align the laryngoscope which enabled the anaesthetist to view the larynx and pharynx.

The anaesthetist was aware of the dangers of aspiration, and that the patient was obese and had missing teeth which he did indeed find made intubation more difficult. Anaesthesia was induced by an injection of sodium thiopentone (STP) and muscle relaxant (4 mg pancuronium bromide (PCB)), and 100 ml suxamethonium (Sux) was injected to enable him to intubate. He soon realised that the patient was having breathing difficulties and was not receiving sufficient oxygen. Remedial action was immediately taken which was not criticised and indeed the patient's treatment at the ITU was described as 'in every way excellent'.

At trial, the plaintiff's case was presented by Dr D.M. Davies, a consultant anaesthetist at St George's Hospital, London. Gastric aspiration could in his opinion have arisen in one of two ways: either because the tracheal tube was placed in the oesophagus instead of the trachea. This was not an uncommon error and Dr Davies accepted that it was not negligent provided it was recognised and corrected immediately. If prompt action is not taken there is an increase of intragastric pressure which could be conducive to the regurgitation of gastric contents. A related hypothesis which was also mentioned was that a tube withdrawn from the oesophagus and inserted into the trachea may bring with it inherent gastric fluid.

Secondly, there could have been a natural escape of gastric fluid from the stomach into the pharynx and thence into the unguarded trachea. The risk of this is greatest after the administration of the relaxant drug which affects all muscles including oesophageal sphincter. If insertion of the tube is difficult, straining of the muscles will increase the likelihood of regurgitation. The plaintiff's expert favoured the second explanation. There was, however, nothing in Dr O's contemporaneous notes to suggest an oesophageal intubation but the plaintiff and her husband were convinced this was what had occurred. This issue was fully explored at trial. The judge said that he was satisfied, having heard all the evidence, that there was no such entry into the oesophagus.

The plaintiff's expert relied heavily upon the order in which the drugs were recorded on the anaesthetic chart, namely:

PCB
STP
Sux

A double-headed arrow was used so that these three drugs aligned with the quantities shown to the left of the chart under the time heading 3.00 hours. The judge said 'If that means that the drugs were administered in the order STP; PCB and Sux, Dr Davies says that Dr O was at fault in using pancuronium in a dosage of 4 mg as the muscle relaxant drug at such a dosage would be insufficient to ensure sufficient relaxation to allow speedy and effective intubation — especially when the patient was obese and missing three front teeth. The subsequent injection of suxamethonium suggested, Dr Davies contended, that Dr O was facing a very critical situation and having only achieved partial relaxation gave suxamethonium (in an appropriate dosage) as an emergency measure.'

The anaesthetist emphatically denied in evidence that he had administered the drugs in this order. He said he had made his entry in his notes during the operation and when the initial problems, which covered not only intubation but dealing with the plaintiff's 'rattling' chest and lack of oxygen intake, were resolved. He said it was not his practice to note the drugs used chronologically. The plaintiff's expert insisted that it is good practice to do this; that drugs should be noted as administered.

Some judicial advice on medical notes

Lord Justice MacDermott dismissed the plaintiff's claim, and accepted the anaesthetist's evidence, and that of the defendant's expert, (Dr King) that no anaesthetist would

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administer these drugs in the order suggested by the notes, and that Dr O had not done this, but he emphasised that it was sensible to note the drugs in the order in which they were administered. This would reduce the risk that the notes would be misinterpreted at a later stage. He said that given the need for speed of intubation, he doubted if absolutely contemporaneous note-making was common practice and thought it was perfectly sensible to 'write-up' the anaesthetic notes when the acute phase of the anaesthetist's function had passed. But he added, '. . . these are notes to be read and understood by anaesthetists dealing with the plaintiff. Good note-taking is for medical purposes, there is no obligation for notes to be written so that they will pass any amount of legal examination at a later date.'

The plaintiff's expert emphasised that there were a number of points on which he would have acted differently to Dr. O the anaesthetist. For example, by bridging the gap in the plaintiff's upper teeth; by sucking out the clear liquid which Dr O saw lying in the plaintiff's pharynx when he began his laryngoscopy; by testing the fluid with litmus paper; and by stopping the intubation when it proved difficult.

It was accepted, however, that such procedures would be very much a matter for the anaesthetist in charge at the time, and the judge said that he was satisfied that in Northern Ireland, good practice did not involve dental bridging as suggested by the plaintiff's expert, so applying the Bolam principle[1] this omission did not amount to negligence. Similarly, it was reasonable to continue the intubation without first testing or sucking out the small pool of liquid. The anaesthetist estimated that intubation took 90–120 seconds; to extend the period further would have increased the period of oxygen deprivation.

In sum, the judge held that difficult intubations were not uncommon and that the anaesthetist had acted properly and competently in dealing with the difficulties that he found. The test to be applied was that of the ordinary skilled man exercising and professing to have that special skill.[2] The anaesthetist could not be blamed for the plaintiff's misfortune.

Modifying the adversarial system in medical negligence claims

In England, there is now a requirement for the exchange of expert reports in medical negligence actions; the 'cards on the table face-up' approach. This does not appear to be the case as yet, in Northern Ireland,[3] but even with the benefits of an exchange of reports, Lord Justice MacDermott's dissatisfaction with the adversarial system is justified. He said 'As 'medical negligence' cases come before the courts in a steady flow I am led to wonder if the existing adversarial system is best suited to their resolution. I would have thought at some early stage after a claim had been intimated a conference between the various doctors concerned could be held and a positive effort made to define the facts. It may be that such a meeting would be assisted by the presence of an independent layman acting as chairman. I would suspect that in many cases when the facts had been fully revealed the plaintiff's advisers would realise that there was no case or the defendant's advisers would realise there was no answer to the claim. Under the present procedure an assessment of liability is postponed for many years during which both the plaintiff . . . and the doctors concerned are bound to have been enduring much anxiety and concern as to the ultimate outcome of the case.

Any new procedure, such as I suggest, will require full and detailed consideration by all those concerned but if rules of court are necessary to give effect to an acceptable procedure I would be disappointed if the legal profession did not support such a change.'

QBD: *Chambers* v *Southern Health and Social Services Board*, Lord Justice MacDermott, 14 April, 1989, [1990] MLR 231.

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Bimanual cricoid pressure

This is a review of the historical basis of our current practice of bimanual cricoid pressure.

Hunter[1] described the use of pressure on the larynx to occlude the oesophagus to prevent insufflation of the stomach during artificial inflation of the lungs 'of persons apparently drowned'. A letter from Dr W. Cullen[2] dated two years' earlier dealt with the same manoeuvre but emphasised a preference for cricoid rather than laryngeal pressure for adequate compression against the cervical vertebrae. One hundred and eighty-five years later, Sellick[3] reported his use of cricoid pressure to occlude the oesophagus to prevent the regurgitation of gastric contents as well as to prevent gastric insufflation. Sellick describes two components to the procedure. These are backward pressure on the cricoid *and* extension of the neck into the sniffing position. Sellick claimed that this extension served to increase the convexity of the cervical spine, to stretch the oesophagus and to prevent lateral displacement of the oesophagus. Compression, as described by Sellick, is generated with downward pressure exerted by the forefinger while the thumb and second finger prevent the lateral displacement of the cricoid ring. Sellick considered that the manoeuvre by an assistant facilitated intubation. Whittington[4] describes the death from aspiration pneumonitis of two women undergoing Caesarean delivery despite the application of crico-oesophageal compression. Sellick describes a two-stage pressure application: moderate pressure applied until consciousness is lost followed by firm

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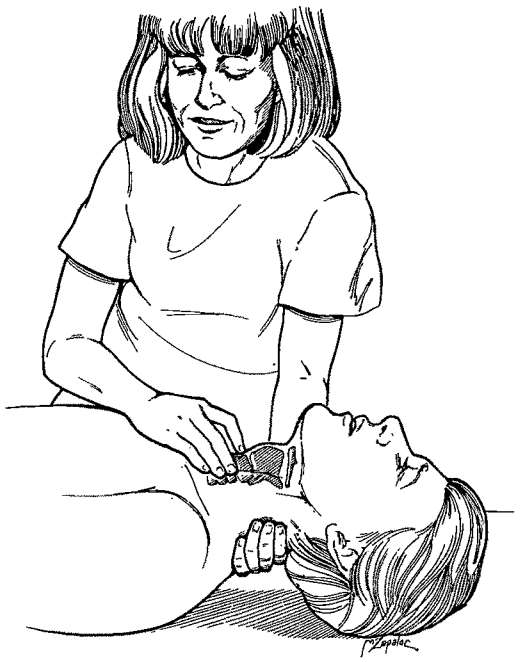

Fig. 1. Assistant's left hand is placed behind the neck lifting up and her right hand is pressing on the cricoid cartilage. The lifting action in the back of the neck places the head automatically in an improved 'sniffing' position. The two-handed technique can be applied in the supine, lateral or any other position.

pressure, but Selwyn-Crawford[5] suggested that cricoid pressure in these cases may not have complied with the recommendations, since pressure was applied when semi-consciousness was achieved rather than beforehand. Adequate pressure must be applied before consciousness is lost and be maintained until tracheal intubation with sealed cuff is complete and confirmed.

Wraight *et al.*[6] determined that a force of 44 N must be applied to the cricoid to be effective protection in the majority of adults. The neck was extended and the head supported during these measurements. His assistants produced pressures between 10.8 N and 120.6 N and the relationship between applied cricoid forces and intraluminal cricopharyngeal pressure was linear. There was also an increase in cricopharyngeal pressure which was attributed to vertebral column extension. The hyperextended vertebral column forms an arch based upon the scapulae fixed below, and a mobile and rotating occiput, above. The cricoid forms the apex of this arch. The integrity of this arch is essential for the best view of the glottis during intubation and the maintenance of an unobstructed airway with a facemask. Disruption of this arch complicates both airway maintenance and laryngoscopy.

The application of significant cricoid pressure in the situation where the neck is extended will tend to collapse the arch by downward apical pressure. The occipital base of the arch rotates and leads to flexion of the head on the neck. The view of the glottis is thus reduced and the tongue blocks the pharynx. Wraight[6] mentions holding the head to help stabilise the arch. Selwyn-Crawford[7] and Miller[8] mention counterpressure with a hand beneath the cervical vertebrae to support the neck. Selwyn-Crawford[9] further describes the use of a 'contra-cricoid' cuboid aid to facilitate extension of the neck as a possible alternative to a bimanual approach.

Bimanual crico-oesophageal pressure has become standard practice here (Fig. 1). It minimises the distortions of the position of the head and the alignment of the trachea which can complicate cricoid pressure performed with one hand. The use of two hands balances pressure, facilitates good 'sniffing' position and helps laryngoscopy and tracheal intubation. Additional precautions must be taken in patients with suspected cervical trauma and fracture, with cervical arthritis and an immobile neck, and in those with laryngotracheal pathology and a compromised airway.

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Cannulation of the posterior tibial artery

Common and well described sites for percutaneous arterial cannulation are the radial, brachial, axillary, femoral and dorsalis pedis arteries. However, these sites may not be available or easily accessible, especially in patients with multiple trauma, burns, or after repeated use.

The posterior tibial artery is a superficial and easily palpable artery that provides an alternative site for cannulation, even in the prone patient. It is easily palpable posterior to the medial malleolus, where it is covered by skin, subcutaneous tissue and the flexor retinaculum. Here it lies, with the posterior tibial nerve on its lateral side, between the tendons of flexor digitorum longus and flexor hallucis longus[1] (Fig. 1). If, in the supine patient, the foot is dorsiflexed to 90° and laterally rotated the artery can be palpated. This may require the knee partially to be flexed.

Palpation is usually at a point one third of the way along a line joining the point of the medial malleolus to the point of the heel. This corresponds to a position near the artery's termination where it divides into the plantar arteries.

A small skin incision is made (using local anaesthesia if appropriate) approximately 0.5 cm distal to this point and in line with the proximal course of the artery. A 20-gauge or 22-gauge cannula can then be advanced through this incision towards and in line with the artery at an angle of

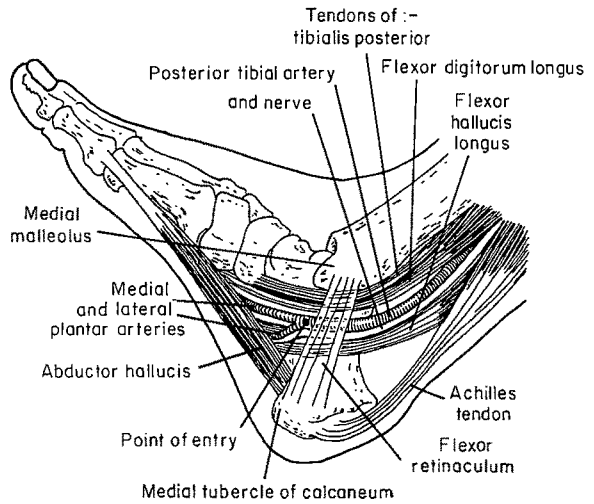

Fig. 1.

approximately 30° to skin, until the artery is entered. Transfixion techniques should be avoided because the nerve may then be hit by the needle.

The foot may be internally rotated or kept in a neutral position in the prone patient. It helps to dorsiflex the foot to 90°.

Cannulation near the bifurcation has two advantages. Firstly, it should enable the cannula to be passed to its full length within the artery before the artery alters its course at its emergence from under the calf muscles. Secondly, the artery is less mobile here since it is stabilised by its two terminal branches.

This site may be a useful alternative to other more recognised sites for arterial cannulation, but formal investigation is obviously necessary to determine its clinical usefulness, the accuracy of pressure measurements taken at this site, the incidence of ischaemic complications, occlusion after cannulation and the incidence of damage to the posterior tibial nerve.

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Detecting awareness during general anaesthesia

It has come to my attention that, in the recent paper by myself and my colleagues (*Anaesthesia,* 1990; **45:** 279–84), the raw data from which the false positive, false negative and predictive values of the various tests for awareness were derived in Table 2 were not included. These may have been of some interest, so I have included them in the accompanying table.

The positive predictive value of a spontaneous lower oesophageal contractility (SLOC) rate of greater than 10 per minute at any time in the first 5 minutes was wrongly quoted as 18% in the original paper. The true value is 26%. This does not make any difference to the overall conclusions.

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Table 1. Specificity, sensitivity and predictive value of different indices of awareness.

Index of awareness	'Deep' positive	'Deep' negative	'Light' positive	'Light' negative	False positive (%)	False negative (%)	Predictive value of positive test (%)
Isolated arm Type 2 movement*	18	47	4	5	28	56	18
SLOC per minute							
>10*	14	51	5	4	22	44	26
>4*	48	17	9	0	74	0	16
PLOC (mmHg)							
>35	18	47	6	3	28	33	25
>13	44	21	9	0	68	0	17
OCI							
>150†	19	46	7	2	29	22	27
>70†	47	18	9	0	72	0	17
	'Aware' positive	'Aware' negative	'Rest' positive	'Rest' negative			
PLOC (mmHg)							
>70	2	0	6	66	8	0	25
OCI							
>270†	2	0	6	66	8	0	25

*At any time in first 5 minutes.
†Mean value over first 10 minutes.

Laryngeal mask and magnetic resonance imaging

Magnetic resonance imaging requires a strong magnetic field that may be either static or dynamic. The region to be investigated must be placed between the poles of the magnet and remain motionless during the imaging. Ferromagnetic material in close proximity to the magnets, movement of the patient, and external electromagnetic

radiation may interfere with the quality of the image produced.

Unwanted electromagnetic interference is eliminated using a metal screen that surrounds the patient lying on the imaging gantry. Isolation of the patient from the ferromagnetic anaesthetic equipment is achieved using extended length gas delivery systems, available from the manufacturers.[1] Patients who are restless require anaesthesia or sedation and must be monitored from a distance, and a clear airway must be guaranteed during the imaging, without the anaesthetist's hands to support it.

The laryngeal mask airway, useful during anaesthesia for magnetic resonance imaging, is made of plastic and therefore has no ferromagnetic properties. It is available in a variety of sizes to suit children and adults, is easy to insert and once in position does not require manual support from the anaesthetist.[2]

Monitoring is difficult in this situation and the laryngeal mask provides a clear airway and an alternative to tracheal intubation with spontaneous ventilation.[1]

Magnetic resonance imaging is increasing in availability and will without doubt continue to do so. Anaesthesia for patients during imaging will become routine and all anaesthetists must be aware of the problems encountered during the procedure. New equipment such as the laryngeal mask airway and modification of existing equipment to operate in areas with a high magnetic field is essential to provide a safe anaesthetic service in an otherwise safe, noninvasive investigation.

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The FEF carbon dioxide analyser

Dr Wee (*Anaesthesia* 1990; **45:** 251), defends his oesophageal detector device (the ODD), against adverse comparisons between its characteristics and those of the FEF carbon dioxide indicator (Fenem Airway Management Systems, New York),[1] and highlights some of the latter's disadvantages in return. It seems to be obvious that neither party is comparing like with like. Both devices appear to perform their tasks admirably, but they are not the same tasks.

The ODD is what its name implies: a detector of oesophageal intubation, and only that. It provides a simple, cheap, reliable and re-usable indication of initial correct tube placement, and is suited for both inside and outside the operating suite. It is not meant to be a continuous monitor. The FEF device, in addition to the initial detection of oesophageal intubation, can remain connected to the tracheal tube, and help detect subsequent tube displacement, respiratory embarrassment, or cardiac arrest (in a similar manner to an end-tidal CO_2 monitor). None of these functions can be done with the ODD. However, at $15 per unit (£13 quoted in the UK) the routine operating theatre use of one disposable FEF device to check each case for oesophageal intubation would be an expensive substitute for the end-tidal CO_2 monitor, or indeed for an ODD.

The FEF device seems to have a major application in intubation at remote locations followed by transfer, as in cardiopulmonary resuscitation. Here detection of correct initial tube placement is vitally important, and both devices seem to be excellent means of verification. However, the extended role of the FEF, as an indicator of cardiac arrest and a check on effectiveness of resuscitation, make it the more useful of the two for cardiopulmonary resuscitation.[2] It may also be useful for transfer of intubated patients where monitoring is limited, as in an ambulance or helicopter. Its ability to monitor continuously is most needed in each of these circumstances, and the single small cost is relatively unimportant.

Incidentally, Dr Wee's assertions that good lighting is essential and that colour-blind users are unable to detect the FEF device colour change are incorrect. The writer is red–green colour blind and has had no difficulty in using the device and not always in good lighting conditions.

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Confirmation of tracheal intubation in a neonate using the Fenem CO_2 detector

We report the use of a Fenem CO_2 detector to confirm correct placement of a tracheal tube in a neonate. This device has a dome colour chart which represents the approximate ranges of end-tidal CO_2 from 0.03% (purple) to 4% (yellow). If connected between the proximal end of the tracheal tube and the anaesthetic breathing system, it can be used in adults to confirm correct placement of a tracheal tube.[1,2] The deadspace of 38 ml has, however, prevented its application during paediatric anaesthesia. When using the Jackson–Rees modification of Ayre's T-piece, this problem can be overcome by placing the detector between the expiratory limb and the open-tailed bag. There is no increase in apparatus deadspace in this position and the low resistance of the device (0.07 kPa at 20 litres/minute) is compatible with the requirements of anaesthetic systems for children.

The patient was a 2-day-old neonate who weighed 1.7 kg and presented for resection of a large cystic hygroma. It was impossible to visualise the larynx and a tracheal tube was passed with great difficulty using a bougie. The baby's lungs were then ventilated by hand using a fresh gas flow of 3 litres/minute. Correct placement of the tube was suggested by chest expansion and bilateral breath sounds audible on auscultation; but it was confirmed by the Fenem indicator which identified the presence of carbon dioxide in the expired gas.

The Fenem no longer indicates the true end-tidal CO_2 since the expired gas is diluted by the fresh gas inflow in the

expiratory limb, but it does provide valuable, rapid confirmation of correct tracheal tube placement.

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Bronchial suction

We read with interest the letter from Dr Shaw (*Anaesthesia* 1990; **45:** 61). Collapse of the lung is reported sporadically, and we also encountered this complication on rare occasions before we started to use selective bronchial suction with a curved-tip catheter with a guide mark.[1-4]

Occurrence of collapse of the lung during anaesthesia is not specific to hemithyroidectomy. What type of suction catheter was used? If the straight tip catheter were used, the catheter would enter the right bronchus at a rate of about 79% because of the anatomy of the bifurcation.[3] Collapse of the left lung might neither be prevented nor resolved by this manoeuvre. We developed a technique of selective bronchial suction with a curved-tipped catheter with a guide mark. Success rates are 94–97% for the left bronchus and 97–100% for the right.[3,4] Thus we have both prevented or treated collapse of the lungs and bronchoscopy has not been necessary for that purpose for the last 11 years. We, however, found that our technique cannot be used for prevention and treatment of atelactasis of the upper lobes[5] and have therefore developed a technique for catheterisation of the upper lobes soon to be reported in this journal.[6] We recommend selective bronchial suction, immediately after intubation, during the course of anaesthesia, if indicated, and at termination of operation before extubation.

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Goldenhar's syndrome

The article by Dr R. Madan and his colleagues (*Anaesthesia* 1990; **45:** 49–52) was interesting. Recently, I was confronted with a similar infant, aged 2 months, who weighed 9.5 kg. Epibulbar dermoids were to be excised. There were also pre-auricular appendages, a high arched palate and a cleft lip. Systematic examination and X ray of cervical spine did not reveal any abnormality.

An intravenous infusion and routine monitoring devices were set up. Anaesthesia was induced with oxygen, nitrous oxide and halothane using the Jackson–Rees modification of Ayre's T-piece. The trachea was successfully intubated, on the second attempt under deep halothane anaesthesia. The electrocardiograph showed bradycardia soon after tracheal intubation. The halothane was switched off and ventilation of the lungs was assisted. Three doses of atropine 0.01 mg/kg were given intravenously at intervals of 2–3 minutes without any effect. Normal sinus rhythm returned as soon as the infant was extubated.

Induction was again tried with oxygen, nitrous oxide and halothane and the trachea was successfully intubated on the first attempt, but bradycardia appeared again which did not respond to intravenous atropine. Normal sinus rhythm returned on extubation. (Nasopharyngeal intubation was avoided in view of high arched palate and fear of bleeding from trauma).

Inhalation induction and tracheal intubation were abandoned and our anaesthetic management consisted of injection of ketamine 1 mg/kg, and a Jackson–Rees modification of Ayre's T-piece was attached to a precut tracheal tube which was inserted with an oropharyngeal airway. Spontaneous ventilation of oxygen, nitrous oxide and halothane continued throughout the procedure, while the airway was supported manually. Surgery, which lasted for about 1.5 hours, was completed uneventfully.

Is it a normal response of infants with Goldenhar's syndrome to tracheal intubation to show resistance to intravenous atropine? Dr Madan did not mention this in his case report.

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A reply

Dr Khan's observation about the resistance of reflex bradycardia to atropine in a patient with Goldenhar's syndrome is interesting. We never encountered any such problems in our series of patients, currently the largest to date. However, there are certain points which we would like to discuss.

The patient referred to by him was a 2-month-old child who weighed 9.5 kg. If it is not a typographical error, on the basis of weight for age it appears that the child was well outside the normal weight range. It does raise the possibility of co-existing disease in this patient.

Dr Khan used doses of 0.01 mg/kg to overcome the bradycardia. Larger doses (0.015–0.07 mg/kg) are recommended by various authors,[1] especially in infants. Moreover, for patients who may require repeated laryngoscopies for intubation, prophylactic use of intravenous atropine is also advised.[2]

Was it possible that the oesophagus was intubated since the bradycardia disappeared and normal sinus rhythm returned after extubation? Confirmation of correct placement of the tracheal tube by observation of chest movements and by auscultation are both unreliable but an end-tidal carbon dioxide monitor is useful.

Why was ketamine used when previous inductions with halothane were uneventful? What was the effect of ketamine on the heart rate of a patient not responding to intravenous atropine?

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P.K. KALIA

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Postdural puncture headache with 29-gauge spinal needles

Clinical experience with 29-gauge spinal needles is limited, but a number of studies suggest that postdural puncture headache either does not occur[1] or is extremely rare[2] when very fine spinal needles such as 29-gauge are used. However, in our experience in the use of these needles in both obstetric and gynaecological patients, we recommend caution when patients are advised about the incidence of headache after such procedures.

We used a 29-gauge Vygon spinal needle in 18 female patients, two of whom developed typical postdural puncture headaches in the early postoperative period. Both patients were relatively young (31 and 33 years) and were to have elective procedures (Caesarean section and cervical cone biopsy). A successful dural puncture was confirmed by the appearance of CSF at the needle hub and by successful spinal anaesthetic blockade. Puncture attempts were atraumatic and required a single approach. The anaesthetic agent used in both cases was 2.5 ml bupivacaine 0.5% and 5% dextrose. Both headaches occurred less than 24 hours later, failed to resolve with conventional therapy and required an epidural blood patch 48 hours after onset of symptoms. The blood patch resulted in immediate complete resolution of the headache.

We are currently undertaking a clinical study to evaluate the incidence of side effects using 29-gauge spinal needles.

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D. FITZGIBBON
J. GARDINER

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Device to maintain the position of a 29-gauge spinal needle

The advantages of 29-gauge spinal needles for spinal anaesthesia in young adults are described by Flaatten *et al.*[1] The use of thin spinal needles is technically more difficult and it is necessary to use an introducer for the 29-gauge spinal needle. If the introducer is inserted too far it can cause dural puncture. The identification of correct placement of 29-gauge spinal needles is confirmed by aspiration of cerebrospinal fluid with a 2-ml syringe, because the spontaneous flow through the thin needle is extremely slow. Dr Tunstall describes a method to maintain the position of the 29-gauge needle by placing a droplet of fluid on the needleshaft.[2]

It is possible to use an ordinary epidural needle as introducer for the spinal needle which must, in that case, be longer than standard size. The advantage of this method is that most anaesthetists are accustomed to detection of the epidural space, and the distance to reach subarachnoid space is short when the introducer is already in the epidural space.

A sharp introducer cannot be inserted so far because of the risk of dural puncture. A sterile disposable spinal-epidural set is available from B. Braun Melsungen with an ordinary epidural needle and a long spinal needle (25-gauge). The spinal needle in this set reaches 1 cm outside the epidural needle when it is inserted completely. The distance needed for penetration from the epidural to the subarachnoid space is variable. A fixation device (Fig. 1) can keep the spinal needle safely fixed to the epidural needle and maintain the same position during aspiration of cerebrospinal fluid and the injection of local anaesthetic. It is possible to adjust the distance of the spinal needle, which extends out of the introducer, and confirm the distance on the device which is fixed to both needles. This device is made of a metal wing and bar with a ring and screws for

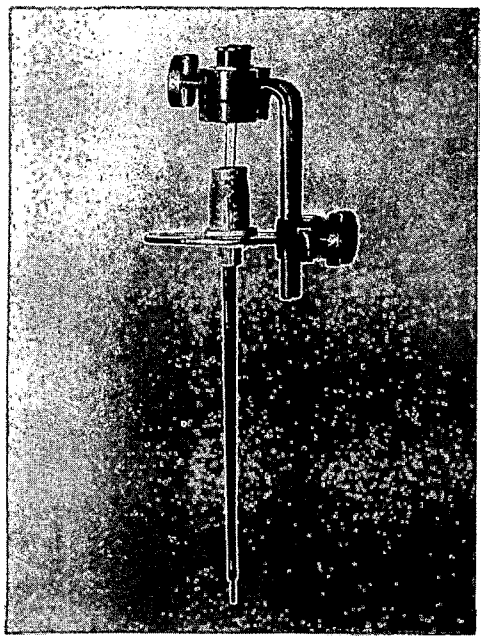

Fig. 1.

fixation. The wing fits to a Portex epidural needle. The spinal needle is fixed to the ring, inserted in the epidural needle and fixed to the wing.

The device for a Becton-Dickinson spinal needle and a Portex epidural needle is available from Narkosspecial, Box 286, 79126 Falun Sweden.

Ludvika Lasarett, J. SIMSA
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Propofol, porphyria and epilepsy

The use of propofol in patients with porphyria is controversial, but it was used in patients with acute intermittent porphyria without ill-effect,[1–4] although porphyrins were not always measured. It appears to be safe in an animal model of porphyria.[5] Increased excretion of porphyrins occurred in a prolonged propofol infusion during orthopaedic surgery in a patient who had variegate porphyria.[6]

A 41-year-old female with epilepsy and porphyria who weighed 65 kg was admitted for diagnostic dilatation and curettage because of menorrhagia. She was diagnosed as epileptic when aged 8 years and from the age of 16 she was said to have porphyria but the type was unknown. In 1988 she had bilateral great-toe osteotomies under spinal anaesthesia and midazolam sedation with no ill-effect. She had never undergone general anaesthesia.

She was well; her last nocturnal fit was one month before admission. She was taking 800 mg carbamazepine daily in divided doses. She requested general anaesthesia. The proposed technique and tests were explained and she gave her consent.

She received no premedication. Anaesthesia was induced and maintained with propofol (total dose 170 mg) and alfentanil (total dose 800 micrograms) while breathing oxygen in nitrous oxide (66%). ECG, blood pressure and oxygen saturation were monitored throughout.

Table 1.

Urine	Porphobilinogen (μmol/litre)	Total porphyrin (nmol/litre)
Normal range	0–8.8	20–320
Before anaesthesia	271	1814
After anaesthesia		
6 hours	221	1663
9 hours	98	454
Plasma	Total porphyrin as uroporphyrin (nmol/litre)	
Normal range	2.2–8.5 (nmol/litre)	
Before anaesthesia	95	
	106	
After anaesthesia		
1 hour	77	
6 hours	72	
18 hours	65	

Her blood and urine samples were analysed before and after anaesthesia (Table 1). Anaesthesia and recovery were uneventful and she was discharged the next day. The results show high levels of porphyrins before anaesthesia with lower levels after anaesthesia. Further analyses were compatible with diagnosis of acute intermittent porphyria.

It is worthy of note that carbamazepine was implicated in causing increased porphyrin production and a condition similar to acute intermittent porphyria.[7]

This case adds evidence that propofol is not porphyrinogenic, but further surveillance is necessary to confirm this.

We thank the Department of Biochemistry, Southmead Hospital and the University Hospital of Wales for their help and advice.

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Coeliac plexus block with alcohol

Coeliac plexus block with alcohol, for malignant visceral abdominal pain, has been used extensively for the past 25 years. Bridenbaugh *et al.*[1] recommended using 40–50 ml 50% alcohol. Moore[2] reported good results in 168 patients after use of this technique.

A case of paraplegia, after a block under X ray control[3] using 6% aqueous phenol, raised the possibility of vascular spasm as the precipitating mechanism. This report, coupled with knowledge of an affinity of phenol for blood vessels,[4] discouraged further use of phenol for this procedure. The use of concentrated solutions of alcohol for coeliac plexus blocks is based on a false premise and is against the advice and judgement of experienced practitioners: the irritant effect of absolute alcohol is well known.[5]

Do we have to wait for more reports of paraplegia before a rational approach to the problem is adopted?

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Tussive effect of fentanyl

The article by Böhrer *et al.* (*Anaesthesia* 1990; **45:** 18–21) was interesting since, in my experience, 60–75% patients who are given fentanyl, sufentanil and alfentanil also cough. Small doses of 50–75 μg fentanyl, 15 μg sufentanil, 500 μg alfentanil, provoke coughing spells before any other drug is given. Another interesting phenomenon is that patients volunteer that they feel tingling, warmth and a slightly tight sensation in the chest which radiates to the extremities in a couple of minutes. Dr Böhrer *et al.* used a big dose as a bolus (7 μg/kg) over one second; it is surprising that they did not encounter any chest wall rigidity and apnoea.

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A reply

We appreciate the comments made by Dr Ananthanarayan which are in complete agreement with our findings. The peripheral injections were done through veins on the dorsum of the hand. Recently, we witnessed three adult patients who had coughing attacks after antecubital intravenous injection of 0.2 mg fentanyl.

Problems with chest wall rigidity or apnoea were minor in our patients because the boluses of fentanyl were always followed by an induction sequence which included pancuronium. Alfentanil given in equipotent doses would undoubtedly lead to chest wall rigidity and apnoea within our period of observation, because the onset of action of alfentanil is much more rapid. Another unwanted side effect of such a bolus of alfentanil would be profound bradycardia. We do not have any experience with sufentanil, so we cannot comment.

We did not observe our patients for a couple of minutes before proceeding with the induction of anaesthesia. We suggest that the symptoms of warmth might be related to slight venous dilatation, which is known to be a common side effect of opioids.

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West Germany

Method-comparison studies: the Keeler Pulsair tonometer

We read with interest the article by Dr Bricker and colleagues describing the use of the Keeler Pulsair tonometer for the peri-operative measurement of intra-ocular pressure (*Anaesthesia* 1990; **45:** 36–9). However, we believe a more rigorous data analysis would have provided further verification of the accuracy of this new instrument.

The authors derive the correlation coefficient together with the estimated least squares regression parameters. This analysis assumes that the x-variable (i.e. the 'standard' instrument) is measured without error, which is not the case for their data. A more appropriate analysis in this situation is that of Deming.[1] Further, the regression analysis described provides little indication of the agreement between the instruments and cannot be used to establish whether the new device is of sufficient accuracy. This is particularly pertinent when a standard clinical technique already exists; in this case, Perkins applanation tonometry. In such method-comparison studies[2] the intraclass correlation is the appropriate statistic for the evaluation of agreement.

We and others[3] believe there exists a frequent confusion between correlation and agreement. It is worth recalling that measurements obtained from two different instruments may be significantly correlated yet the absolute agreement may be so small as to render the candidate instrument clinically worthless. In the absence of sophisticated analyses, readers can be greatly assisted if authors state the percentage of observations obtained with new instruments which fall within chosen bandwidths of those obtained with the 'gold standard' (e.g. in the case of intra-ocular pressure, ±1 mmHg, ±2 mmHg, ±3 mmHg).

Birmingham and Midland Eye Hospital, M.J. MOSELEY
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A reply

We are grateful for these comments. It is our understanding that the statistical analysis described does not in fact assume that the x-variable is without error, and we are assured that the correlation coefficient is appropriate for the determination of the accuracy of the instruments in respect of each other. However, we acknowledge that measurements obtained from two different instruments may be significantly correlated yet absolute agreement may be small. We remain uncertain how to apply intraclass correlation tests to data that derive from groups that are not subdivided. We accept that to state the percentage of results that fall within given bandwidths is a simple and better way of presentation, although some would argue that the use of predictive error variance is preferable. It is clearly important to use appropriate statistical tests, but the sophistication of the analysis should also match the stated aims of the study. The accuracy of the Keeler Pulsair tonometer has already been established by various workers, and as long ago as 1974:[1] our purpose, as outlined in our introduction, was not to replicate their figures but to determine the suitability of the instrument for peri-operative measurement of intra-ocular pressure by non-specialists. This we believe we have achieved.

Royal Liverpool Hospital, Liverpool L7 8XP — S.M. MOSTAFA
Arrow Park Hospital, Wirral — S.R.W. BRICKER
University of Liverpool — D.S. PERCY

Reference

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Mitochondrial myopathy and anaesthesia

The case report and review of anaesthesia for patients with mitochondrial myopathy by Drs Burns and Shelley (*Anaesthesia* 1989; **44:** 975–7) was particularly timely since we were asked to anaesthetise a patient with the condition within days of reading the article. The response of patients with this myopathy to non-depolarising agents is not previously reported. We used atracurium as part of the anaesthetic technique with no untoward effects.

The patient was a 26-year-old man who presented for bilateral intranasal antrostomies and turbinectomy. He was known to have a mitochondrial myopathy since the age of 14 years. His precise metabolic abnormality was the subject of previous case reports.[1,2] The only symptom referable to his myopathy was weakness after exertion. Physical examination showed a young man, 170-cm tall, but who weighed only 43 kg, with ophthalmoplegia and obviously abnormal wasted muscles. His electrocardiogram showed a previously undiagnosed Wolff–Parkinson–White syndrome.

We elected to use an anaesthetic technique that involved paralysis and ventilation rather than use volatile agents breathed spontaneously through a tracheal tube. We were, however, concerned about the unknown response to non-depolarising relaxants.

Premedication was with oral temazepam and intravenous verapamil. Anaesthesia was induced with propofol and maintained with an infusion of propofol and 66% nitrous oxide in oxygen. Neuromuscular function was monitored with a nerve stimulator with electrodes applied over the ulnar nerve. The train-of-four response was unaffected by a small dose of atracurium (2 mg) and a further 20 mg was given which resulted in abolition of all four twitches and good conditions for tracheal intubation. Two twitches had returned spontaneously by the end of surgery 20 minutes later and residual neuromuscular blockade was reversed satisfactorily with neostigmine 2.5 mg and glycopyrronium 0.5 mg. The ECG showed sinus rhythm throughout.

Our experience suggests that the pharmacodynamics of atracurium are not altered in mitochondrial myopathy, although caution and neuromuscular monitoring remain prudent.

Princess Margaret Hospital, Swindon SN1 4JU — A. KELLY, M. O'CONNOR

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A reply

Thank you for giving us the opportunity to reply to the comments of Drs Kelly and O'Connor.

We are pleased that they found our report of a patient with mitochondrial myopathy useful and are interested in their use of atracurium in another patient. We considered that atracurium was the neuromuscular blocking agent of choice but that only by monitoring neuromuscular function could it be used safely. Their patient did not appear to be sensitive to atracurium but we agree that monitoring neuromuscular function remains the safest way to administer neuromuscular blocking agents to patients with a documented myopathy.

University Hospital of South Manchester, Withington, Manchester — M.P. SHELLY
Addenbrooke's Hospital, Cambridge — A.M. BURNS

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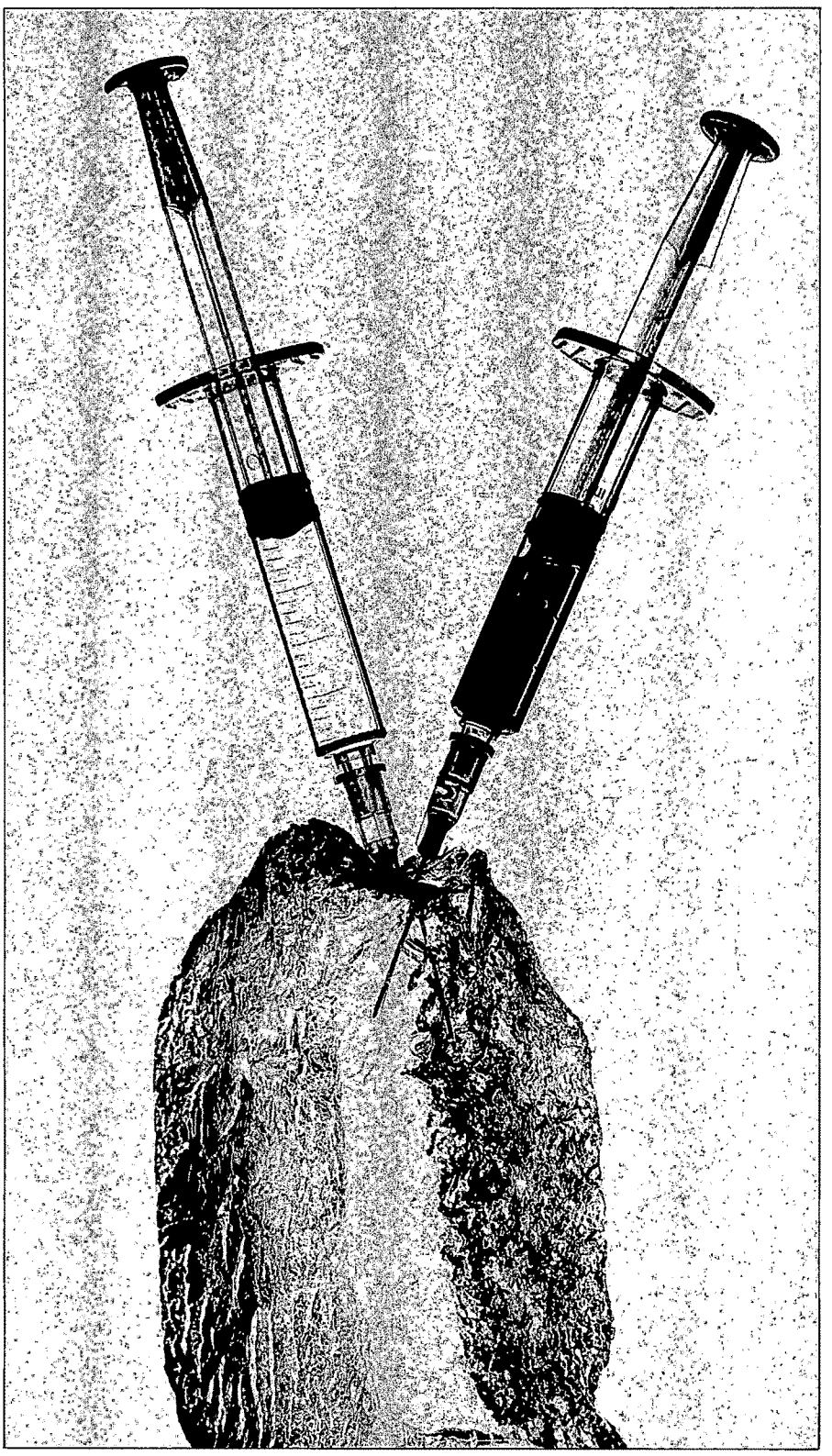

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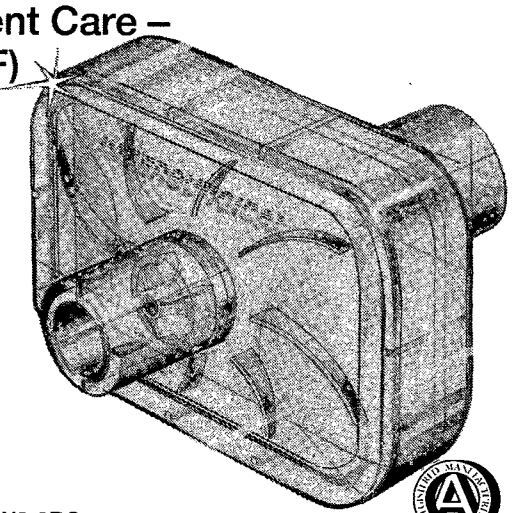

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Problem with the Vapor vaporizer

A 25-year-old woman was anaesthetised for gynaecological dilatation and curettage. Induction was with 0.1 mg fentanyl and 250 mg thiopentone, and anaesthesia was maintained with nitrous oxide 66% in oxygen via facemask and a modified Mapleson C system. Halothane was added to the inspiratory gas mixture with dial settings of 1.5 to 2% on a halothane Vapor (19.3) vaporizer (Drägerwerk AG, Lübeck, FRG). The patient developed severe laryngeal spasm with subsequent cyanosis on insertion of a vaginal speculum; suxamethonium 50 mg and manual ventilation of the lungs with 100% oxygen was required. A vaporizer malfunction was suspected and confirmed with a Capnomac Anaesthesia Multigas Monitor (Datex, Helsinki, Finland).[1] Readings showed that, at any vapour concentration setting, no vapour was delivered to the inspiratory gas mixture.

The Dräger 19.3 Vapor is a temperature- and pressure-compensated vaporizer based on the dilution-bypass principle. The vapour concentration delivery is controlled by variation of a cleft between a cone and its (female) counterpart which changes the flow ratio through the vaporizing chamber. The construction of the dosing system ensures automatic cut-off of the vaporizer output by closing down the dosing cleft when high external accelerating forces equivalent to 250 g affect the vaporizer. The fresh gas flow is not affected by this cut-off. The cut-off of vaporizer output should avoid delivery of excessive vapour concentrations to the patient.

Two remarks can be made about this safety control mechanism. First, we could repeatedly demonstrate that this automatic closing mechanism occurs if the vaporizer is tipped over. Secondly the activation of this safety mechanism can only be detected by a slight decrease of resistance to turning the concentration knob and a discrete broadening of the cleft between the concentration handwheel and the vaporizer body. We also noticed that a simple vertical blow on the dial handwheel restores normal vaporizer output.

This may represent more than just a theoretical problem. Agent-specific vaporizers, like the Dräger 19.n series for halothane, enflurane and isoflurane, are frequently used with a plug-in system for rapid interchange of the volatile anaesthetic agent. However, frequent change of vaporizers increases the risk of damage or tilting. We are concerned about the sensitivity of the safety closing mechanism and, more importantly, the poor warning of this. It may be unnoticed. Thus adequate surgical anaesthesia might not be obtained with possible harmful effects to the patient. Furthermore, patients may be exposed to the psychological sequelae of unexpected awareness during surgery.

We consider that the mechanism whereby the Dräger 19.3 vaporizer output is cut off after a shock or a tilt, occurs without adequate warning. Broadening of the cleft between concentration dial ring and vaporizer body together with discrete loss of resistance on turning the concentration dial ring can be difficult to appreciate, and does not provide an adequate warning of vaporizer malfunction. Any dysfunction or malfunction of a vaporizer, which causes a vapour concentration either in excess or below that indicated by the dial setting, should have a reliable warning. When available, an inspiratory vapour concentration monitor can be used in combination with Dräger 19.n vaporizers to avoid unexpectedly light anaesthesia.

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J.J. Driessen
J.M.L.G. Eerens
G. van Hoonacker

A reply

The Dräger Vapor 19.n is a precision instrument that works on the bypass principle and meters the gas flow through the vaporizing chamber between 2 ml/minute and 3500 ml/minute. This change in gas flow is achieved mechanically by variation of a slot which is formed by a cone and a correspondingly formed counterpart. The variations are in the micrometer range.

It cannot be excluded that due to mechanical stress, which may not be recognisable from the outside, there is damage inside the vaporizer that might have led to a change in the mechanical geometry. A different concentration might then be delivered.

Since, as in this case report, an inadmissible increase of the supplied anaesthetic concentration cannot be excluded, the metering device was designed so that after a shock the Vapor 19.n switches off the concentration supply and maintains the fresh gas flow. This condition may be recognised by the reduced frictional resistance when the handwheel is turned or on the display of an anaesthetic gas monitor.

This is not a malfunction. It is a necessary safety mechanism which becomes effective when the Vapor is exposed to deceleration for example by dropping during routine clinical care. This may be recognised during the pre-use check. We do not know of any case in which the delivery of anaesthetic agent was suddenly switched off during anaesthesia. Our experience is that simply tipping the Vapor 19.n does not result in a cut off but it might be that this instrument was already damaged and we therefore assume that it was defective.

The anaesthetic vaporizer Dräger Vapor 19.n is designed such that the decelerations occurring during usual clinical application, handling and transport do not influence the function of the instrument.

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W. Falb
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Analgesia after haemorrhoidectomy

Dr S.J. Pryn (*Anaesthesia* 1989; **44:** 964–6) has suggested the addition of small amounts of opioid to caudal local anaesthetic to improve postoperative analgesia for haemorrhoidectomy. We have compared caudal morphine with lumbar epidural morphine 2 mg in 10 ml saline for Milligan Morgan haemorrhoidectomy. The selection of patients for surgery was the same as in Pryn's study. Bowel preparation consisted of oral magnesium hydroxide and ispaghula husk and a phosphate enema. The surgeon infiltrated the area with 10 ml plain lignocaine 1% before operation. The general anaesthetic technique was identical to that described by Pryn. The morphine was administered after induction of anaesthesia and nine patients were randomly allocated to each group. Recording of pain

Table 1.

	Lumbar group ($n=9$)	Caudal group ($n=9$)	Probability
Patients who required analgesia in recovery	1	5	ns
Patients who required analgesia over first 6 hours	1	6	<0.05
Patients who required analgesia over first 24 hours	3	8	<0.05
Mean number of requests for analgesia (per patient per 48 hours)	1.5	2.7	
Mean time to first bowel action, hours	56	73	ns
Mean time to first bowel action, hours, all patients		64	

scores was undertaken by nurses who did not know which technique had been performed, and scored on a 100-mm linear analogue scale.

It was reported that the patients who had received caudal morphine were not as comfortable in the immediate postoperative period as those who had received lumbar epidural morphine. Unfortunately, we had made no provision in our study design for the subjective assessment of pain until 4 hours after the operation. A difference between pain scores (34 in the caudal group and 10 in the lumbar group) did not reach statistical significance by this time. Assessments at intervals up to 32 hours revealed similar findings.

More patients in the caudal group required analgesia than did patients in the lumbar group. The table shows the results and the results of analysis with Fisher's exact test. There was no correlation between the number of doses of postoperative analgesia and the time to bowel opening.

Pryn suggests that addition of opioid to caudal local anaesthetic may improve pain relief in the immediate postoperative period. Our study suggests that he will be disappointed if he uses a dose as low as 2 mg morphine. We noted that any beneficial effect that caudal morphine might have had was not noticed over the first 4 hours. Lumbar morphine reduced the requirement for supplementary analgesia and provided effective analgesia from the time of awakening in the majority of patients.

The administration of opioids via caudal epidural injection is convenient to perform if caudal local anaesthetic is being administered. However, the caudal approach to the epidural space deposits the opioid at a site distant from that at which it is believed to work, and it may not be logical to administer opioid in this manner. Caudal opioids have been the subject of several studies in adults, but such studies have involved doses up to 10 mg morphine, have not studied comparable groups of patients and have not compared caudal with other routes of epidural administration.[1,2] It is claimed that there is a specific segmental effect of caudal opioids on the sacral nerve roots. Our study does not support this claim.

It is disappointing that the use of epidural morphine in our study was associated with a prolongation in the time to first bowel opening when compared with Pryn's study. Is it possible that epidural morphine slows the recovery of bowel function? It is not possible to answer this question without more specific information about patients' bowel habits and more rigorous standardisation of techniques than can be achieved in studies being performed by different operators and investigators, but it is a question that needs to be answered.

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A reply

Severn and Khwaja criticise our suggestion that it would be interesting to study the effect of the addition of opiates to bupivacaine caudals for haemorrhoidectomy; they appear to prefer the lumbar route. They used extradural morphine (2 mg) to provide analgesia after haemorrhoidectomy, comparing the caudal versus the lumbar epidural routes. The lumbar administration provided an opiate-sparing advantage but there was no statistically significant analgesic benefit in their small group of patients.

We identified a puzzling group of patients: 23% of those who received a bupivacaine caudal complained of pain immediately postoperatively, yet they appeared to have had a fully functioning block intra-operatively. They tolerated anal dilatation without reflex responses, whilst anaesthesia was maintained with only a low concentration of enflurane. It was to reduce the incidence of this failure that we suggested a further study to determine the efficacy of combining an opiate with the bupivacaine.

Severn did not use a mixture of opiate and local anaesthetic in the epidural space. Pybus *et al.*[1] and Boskovski *et al.*[2] have reported the use of such mixture via the caudal route. Pybus found that the addition of 4 mg morphine to a 2% lignocaine caudal provided significantly better analgesia after haemorroidectomy, with lower pain scores, less opiate requirement and longer duration of action. However, their study was complicated by the routine use of opiate premedication, and the exclusion of an unspecified number of patients in whom a complete block was not verified, perhaps the very patient group which we are highlighting for further study. Boskovski, in an uncontrolled study, found that of only six haemorroidectomy patients given a caudal with 2 mg morphine in 0.5% bupivacaine, all were pain free for 7–9 hours. Thus neither of these two studies, nor that reported by Severn, shed any light on the suggestion that the addition of opiates to a bupivacaine caudal may reduce the puzzling incidence of immediate postoperative pain despite an apparently functioning sacral blockade.

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Frequency of stimulation and twitch height

Dr Bayly (*Anaesthesia* 1990; **45:** 171) believes he has discovered a limitation in the performance of the Bard Biomedical Digital Nerve Stimulator in that repetition of the train-of-four stimulus every 12 seconds reduces twitch height compared with that after longer intervals. This is surely a demonstration of the inverse relationship between twitch height and the frequency of stimulation, one of the characteristics of non-depolarising block. Progressively increasing the rate from 0.1 Hz to 1 Hz can reduce the response by a factor of 2 to 3 and, although a stimulus of 0.1 Hz is usual when potency values such as the ED_{95} are determined, even after a 10-second interval, the twitch height is still influenced by the preceding stimulus. This standard represents a compromise between fade and the practicality of quantification during a rapidly changing neuromuscular blockade, for example, before intubation.

Electronic causes such as a flat battery or a stimulus varying below supramaximal can easily be eliminated as causes, since both the battery voltage and the stimulus current are displayed. The Bard therefore has a better performance than stimulators that lack these features.

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Atracurium infusions without neuromuscular monitoring

The use of atracurium infusions without monitoring neuromuscular blockade was previously reported.[1] We studied a similar technique and evaluated the safety of spontaneous recovery after such a technique.

Thirty patients ASA grade 1 and 2 for various operative procedures were studied. Pethidine and promethazine were given as premedication and anaesthesia consisted of thiopentone, halothane and nitrous oxide in oxygen. Tracheal intubation was carried out after a bolus dose of atracurium 0.6 mg/kg and and infusion of atracurium 0.4–0.6 (mg/kg)/hour was commenced after 20 minutes. The rate was increased, as required, to maintain adequate relaxation. The infusion was stopped approximately 20 minutes before the end of the operation and neuromuscular blockade was reversed with neostigmine 2.5 mg only if recovery of muscle power was not clinically satisfactory. All patients were closely observed in the recovery ward for an hour and discharged to the general wards after assessment by the anaesthetist.

Adequate relaxation as assessed by the anaesthetist and surgeon was achieved in all patients. The infusion rate varied from 0.4 to 0.6 (mg/kg)/hour. Four patients required adjustment to the infusion rate. Adverse effects such as bradycardia, hypotension and bronchospasm occurred in seven patients, all of whom responded rapidly to treatment. Nineteen patients recovered spontaneously from neuromuscular blockade while neostigmine induced rapid recovery in the other 11 patients. All patients recovered fully in the recovery room. No evidence of inadequate reversal was noted.

Atracurium has a rapid plasma clearance and doses are required every 10–15 minutes as increments. Uneven relaxation may also result unless these doses are given at the appropriate time. We found that the use of an infusion avoided these situations and at the same time did not require additional monitoring. Our study also showed that it is possible to allow spontaneous recovery safely after the use of atracurium based on clinical observations alone, although we believe that it would be safer and more appropriate to administer a reversal agent unless specifically contraindicated.

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Reference

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Extraordinary oxygen pipeline failure

Recently an episode occurred when the pipeline oxygen supply to the anaesthetic machine was accidentally interrupted. Two hours into an uneventful anaesthetic the low pressure oxygen alarm on the anaesthetic machine sounded. The reserve oxygen cylinder was immediately turned on to ensure continuation of the oxygen supply to the patient. The inspired oxygen and oxygen saturation devices showed no change in recordings. A tug test on the pipeline showed it was secure, as it had been on routine testing of the anaesthetic machine before the list. However, the pipeline supply failure alarm on the wall had been illuminated. Subsequent investigation revealed that construction work on a building next to the theatre block had required the passage of cabling through fixed channelling in the wall. This had disrupted the valve on the oxygen supply pipeline and caused it to close completely.

Guidelines exist so that work on pipelines is not undertaken except by authorised specialists.[1] The work was not associated on this occasion with the operating theatres but caused a potential hazard. There were no sequelae and warning systems were effective. The audible oxygen supply failure alarm activates on the anaesthetic machine when the pipeline pressure decreases to 50% of normal,[2] or to 18 kPa[3] whichever is the higher. This alarm functioned correctly in this case. However, there was no audible alarm on the pipeline to indicate the location of the failure.

This episode reinforces the need for adequate auditory and visual alarms on the oxygen supply system as well as those present on the anaesthetic machine. Oxygen pipeline failure can occur at any time, so full oxygen cylinders must always be attached to the anaesthetic machine and a routine pre-anaesthetic check of the machine is mandatory.[4] The use of oxygen analysers to monitor the inspired oxygen concentration and pulse oximeters are essential,[5] but would be a much later indication of oxygen supply failure.

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Treatment of extravasation injury

Extravasation of intravenous drugs and infusions can cause serious soft tissue loss and scarring around nerves, joints and tendons.[1–4] Anaesthetists who work in theatre and intensive care, and perform cardiopulmonary resuscitation, are likely to see this complication relatively frequently.

A variety of regimens are currently advocated: topical application of ice,[5,6] injection of hyaluronidase,[7] local injection of steroid to combat inflammation,[8] injection of small amounts of saline to dilute the toxic agent (clysis)[9] and injection of specific antidotes such as phentolamine in the case of extravasation of vasopressor agents.

It is worrying to permit a potentially harmful material to remain in the subcutaneous perivenous space whether diluted, cooled or treated with a specific antidote. Early surgical debridement and skin grafting was recommended[10,11] but it is not possible to predict at an early stage whether or not a soft tissue complication will occur. It is preferable to remove recently extravasated material without resort to skin excision. This can be achieved by infiltration of the area of extravasation with hyaluronidase and the construction of several exit stab wounds around the zone of extravasation. Normal saline is flushed through the subcutaneous space to cleanse it. A liposuction cannula is then inserted and some or all of the extravasated material and subcutaneous fat is sucked out. This can simply be performed under a brachial plexus block. The vasodilatation induced by the latter may also help to prevent tissue ischaemia and accelerate vascular absorption of the extravasated substance.

We have observed the effectiveness of this treatment in patients in whom highly irritant cytotoxic drugs, electrolyte solutions (potassium, calcium) and concentrated parenteral nutrition fluid had extravasated. The patients were referred and treated on the day of the extravasation. Hand function is preserved and skin ulceration prevented in all cases. There is no evidence of any soft tissue damage.

We emphasise the importance of referral of extravasation injuries to a plastic surgeon at the earliest possible opportunity because of the unpredictability of even the most trivial of extravasations. A wait-and-see policy runs the risk that established tissue necrosis and irreversible soft tissue damage will develop.

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Beta-adrenoceptor blocking agents and anxiolysis

Drs Jakobsen and Blom have now reported two studies on the effectiveness of the oral anxiolytic premedicant combination of diazepam 15 mg with metoprolol 100 mg (*Anaesthesia* 1989; **44:** 249–53 and 1990; **45:** 40–3). They found that the beta-adrenoceptor blocking agent enhanced the reduction in anxiety and improved the demeanour of the patient before induction.

Interestingly, their Scandinavian patients mark the 10-cm visual analogue scale for anxiety *before* any intervention at a point below which many British patients would score *after* anxiolytic premedication. This cultural difference may obscure genuine anxiety however, since we note that the researchers' ethics committee required the benzodiazepine component to be included in the study protocol.

We have examined the usefulness of another betablocker used as the sole premedicant in a patient population likely to benefit from minimal residual sedation after operation.[1] Timolol 10 mg was especially effective in the more anxious patients, and reduced indices of anxiety to the level of those who denied anxiety. The dose of propofol required for induction was significantly reduced in those given timolol, and cardiostability during anaesthesia was notably superior. It is not sedative and has a long half-life so timolol can be given early on and yet not add to nursing care. Patients who have procedures under local anaesthesia

may also benefit from this form of anxiolysis without compromise to their street-fitness, and in children's day-cases it might be useful for anxious parents!

We agree with the findings of Drs Jakobsen and Blom that the combination provides the greatest anxiolysis, but point out that beta-blockers alone can provide useful anxiolysis when sedation is considered undesirable.

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Reference

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A reply

Drs MacKenzie and Bird comment on issues concerning both the results and the method in two of our studies. The difference in perceived anxiety (marking on a 10-cm visual analogue scale) between our study and theirs can be explained by several factors. There may of course be a cultural difference between Danish and British patients, but the use of visual analogue scales can be very troublesome to handle and comparison between studies is difficult.

There are numerous problems with the visual analogue scale method: for example the prefixes, those remarks of the investigator and the patients' interpretation of them. Secondly, the cultural, social, educational and ethical differences; it is difficult for patients to judge their anxiety reliably; they may be reluctant to express anxiety to an unknown person, and find it difficult to express their feelings. There are problems concerning the interpretation and statistics of the defined points on the scale: is the distance between 10 and 30 mm the same as that between 30 and 50 mm? We found some differences between the observers' rating and the patients' rating in our studies, so the difference between the studies may be smaller.

Drs Mackenzie and Bird point out that our patients were premedicated with diazepam. When we started our study, to our knowledge, no information was published on beta-adrenoceptor antagonists as premedication, which was the reason for using metoprolol together with diazepam. This probably results in smaller difference between the group receiving metoprolol and the control group.

We find the information on the effectiveness of a sole beta-adrenoceptor antagonist very promising. We have found that pre-operative betablockade reduces bleeding during surgery, the amount of halothane during anaesthesia and the incidence of arrhythmias,[1] but the possible combined effect of a beta-adrenoceptor antagonist and cardiodepressive effect of different anaesthetics had to be explored further.

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An accident with the Lack system

The importance of a thorough check on all anaesthetic equipment before use is illustrated by this recent incident.

A Lack (co-axial Mapleson A) system was briefly checked. A visual inspection revealed no obvious fault. A test for leaks by closure of the expiratory valve, occlusion of the distal end with a thumb and compression of the filled reservoir bag caused no significant leak. It was apparent that the internal diameter of the distal end was too large when one attempted to connect the system to the catheter mount attached to the tracheal tube of the the first

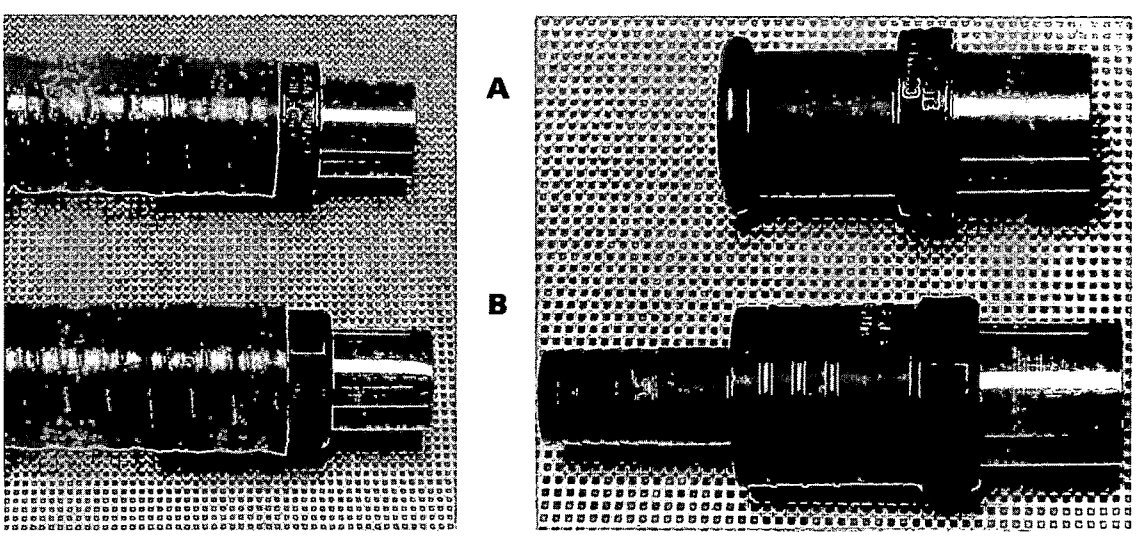

Fig. 1. A. the customary arrangement. B. the accidental arrangement.

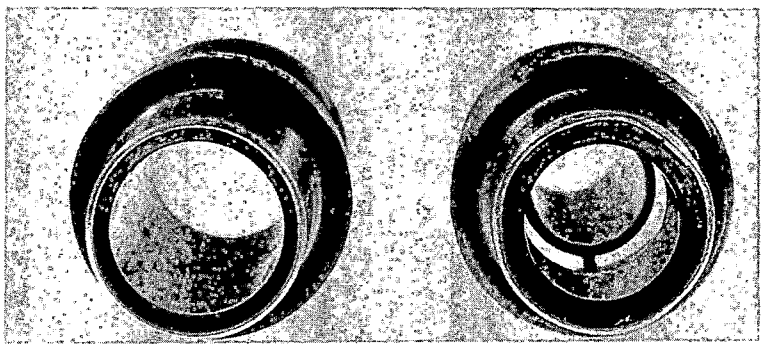

Fig. 2. This shows how the inspiratory tube of the Lack system may be blocked.

patient. Furthermore, it was impossible to ventilate the patient's lungs. The breathing system was replaced and anaesthesia continued uneventfully.

The inner lumen was found later not to be obstructed but it was clearly impossible to ventilate through it. The larger-than-normal internal diameter of the distal end warranted further attention. When it was removed the fault became obvious. A reservoir bag mount had been inserted into the distal end (labelled A). This had the same external appearance as the normal arrangement (labelled B) but is clearly not suitable since it occludes the outer inspiratory limb of the Lack system. When checking this system, and indeed all systems, it is important to ensure that all parts to be connected are compatible, to check both the inspiratory and expiratory limbs for leaks and to ascertain that the patient can be adequately ventilated.

This report serves to emphasise not only the importance of a thorough equipment check by also the danger of parts that are easily interchangeable.

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Other information from the strain gauge transducer

Proximal intratracheal pressure and lung compliance measurements are well established methods for ventilatory monitoring.[1]

We report the construction of a device, based on the common strain gauge transducer, which is easy to assemble, inexpensive, readily available at the operating room, and quite reliable.

Figure 1 shows the arrangement. Connexion is made between the angle piece of a tracheal tube, (Rowbotham swivel adaptor, Portex model) and the transducer (GF). A nasogastric suction tube (D), (Vygon CH 12), with a soft, proximal end (C), is convenient using the hub (E) of an intravenous catheter 12-gauge with the Luer-lock adapter and the intravenous part entirely removed.

The transducer is zeroed and then the proximal pressure (PIP) can be recorded. Figure 2 shows the analogue tracings.

Approximate values for total compliance (C), can be obtained, at the moment of an inspiratory pause: $C = V_T/P_{IP}$.

Sometimes, the inspiratory pause is too short, and a reading at zero flow is not possible. This phase, can be prolonged by occlusion of the exhaust at the moment of the expiration (Fig. 2E). Care must be taken with filters. Frequencies greater than 3 Hz should be rejected (Fig. 2F).

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Reference

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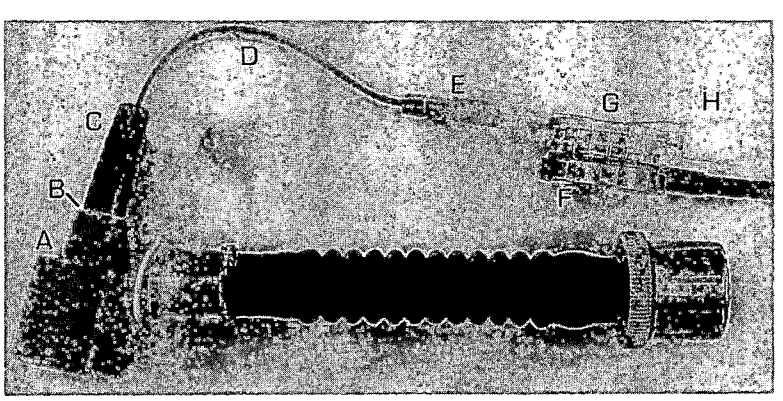

Fig. 1. Assembled device.

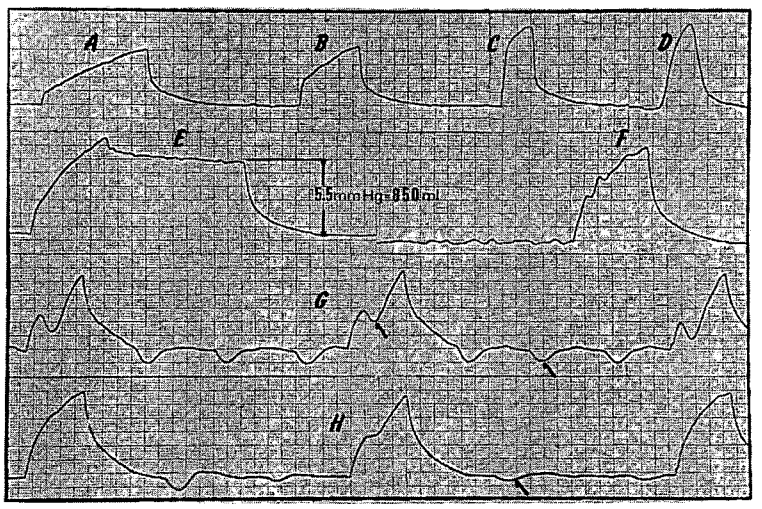

Fig. 2. Recording examples (paper speed: 25 mm/sec): A, low fresh gas flow; B, medium gas flow; C, high fresh gas flow; D, manual (with bag) ventilation; E, artificial inspiratory pause; F, noise on the recording; G, subclinic hiccoughs, not noticed by the surgeon (arrows); H, decrease in amplitude of hiccoughs, after 2.5 mg/65 kg, alcuronium.

Erratum

Anaesthesia, 1990, Volume 45, page 414

Postspinal headache

The first sentence of this letter by N. Weksler and L. Ovadia should read:

> We read with interest the excellent article by Rasmussen *et al.* (*Anaesthesia* 1988; **44:** 571–3) in which postspinal headache incidence was compared after the random use of 20- or 25-gauge needles in elderly and young patients.

Anaesthesia, 1990, Volume 45, pages 604–611

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents–Life Sciences* for February 1990. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

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Morphine and metabolite behavior after different routes of administration: demonstration of importance of active

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The collator of this section is Dr L. Kaufman, MD, FFARCS, 145 Harley Street, London W1N 2DE. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase II, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

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Treatment and medication

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Central nervous system

Physiology

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Treatment and medication

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Endocrine and metabolic

Physiology

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Treatment and medication

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Pain

Physiology

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Treatment and medication

Opiates and peptides. CHRUBASK J. In: LIPTON S *et al.* eds. *Pain clinic*. New York: Raven Press, 1990: 349.

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Other

Treatment and medication

Therapeutic management of nausea and vomiting. MARIN J, IBANEZ MC, ARRIBAS S. *General Pharmacology* 1990; **21:** 1.

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Obituaries

Faux, N.I., FCAnaes, DPH, formerly Consultant Anaesthetist in Rhyl. Qualified from University of London in 1934.
Grenville, H., MRCS, LRCP, FFARCS, DA, formerly Consultant Anaesthetist at the London Hospital Group. Qualified from University of London in 1940.
Davidson, J.T., MD, FFARCS, formerly Professor of Anaesthesia, Haddassah University, Jerusalem.
Lucas, M.G.L. MB, ChB, LRCP, MRCS, LRFPS, FFARCS, DA, formerly H.M. Coroner, Co. Beds. Qualified from University of Edinburgh in 1922.
Longstaff, S.E.A.F., MB, BS, FCAnaes. Qualified from University of Newcastle in 1982.
Mortell, A., MB, BCh, FFARCS, DA, formerly Consultant Anaesthetist, United Birmingham Hospitals. Qualified from National University of Ireland.
Overton, P.M., MB, BCh, FFARCS, DA, formerly Consultant Anaesthetist Bolton and District Group of Hospitals. Qualified from University of Leeds in 1923.
Powell, K.J., MB, BS, MRCS, LRCP, FFARCS, DA, formerly Consultant Anaesthetist at Royal Devon and Exeter Hospital. Qualified from University of London in 1938.
Rice, R.A.C., MB, BS, MRCS, LRCP, FFARCS, DA, formerly Consultant Anaesthetist at United Norwich Hospitals. Qualified from University of London in 1930.
Robertson, J.D., MD, MB, ChB, FRCP, FRCS, FFARCS, formerly Professor of Anaesthetics, University of Edinburgh. Qualified from University of Edinburgh in 1940.
Turner, J.T., MA, MB, BChir, MRCS, LRCP, FFARCS, DA, formerly Anaesthetist N. Staffs Group of Hospitals. Qualified from University of Cambridge in 1935.

International congress calendar

1990

18–21 July. London. *First International Conference. Anaesthesia and Critical Care in Disasters and War.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

22–24 August. Edinburgh. *Edinburgh Anaesthesia Festival.*
Information: Dr C.J. Sinclair, Department of Anaesthetics, Royal Infirmary, Edinburgh, EH3 9YW.

3–7 September. Antwerp. *XXXII International Congress for the History of Medicine.*
Information: Thierry Appelboom, MD, Erasmus University Hospital, route de Lennik 808, 1070 Brussels, Belgium.

5–7 September. Berne. *9th Annual Meeting of the European Society of Regional Anaesthesia.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

5–8 September. Budapest. *Third International Symposium on Anaesthesia for Cardiac Patients.*
Information: Mount Sinai School of Medicine, Department of Anesthesiology, 1 Gustave L. Levy Place, Box 1010, New York 1002906574, USA.

9–15 September. Warsaw. *VIIIth European Congress of Anaesthesiology.*
Information: The Organising Committee, VIIIth European Congress of Anaesthesiology, c/o The Polish Society of Anaesthesiology and Intensive Therapy, ul. Kasprzaka 17a, 01-211 Warsaw, Poland.

15–26 September. Interlaken, Switzerland and Munich. *A Comparison of European and American Anesthesia Practices.*
Information: Holiday Seminars, Route 1, Box 30, Goodlettsville, Tennessee 37072, USA.

22 September–7 October. Munich, Berchtesgaden, Graz and Vienna. *A Comparion of European and American Anesthesia Practices.*
Information: Holiday Seminars, Route 1, Box 30, Goodlettsville, Tennessee 37072, USA.

23–28 September. Seoul. *8th Asian/Australasian Congress of Anaesthesia.*
Information: Department of Anesthesiology, Seoul National University Hospital, 28 Yungun-Doug, Chongro-Ku, Seoul 110, S. Korea.

25–28 September. London. *Ultrasound Angiography.*
Information: The Conference Secretariat, P.O. Box 15, Eastleigh, Hampshire, SO5 5XG.

25–29 September. Milan, Italy. *XIV International Congress of European Association of Poison Control Centres.*
Information: Congress Studio, Via Cappuccio, 19-20123 Milano, Italy.

26–28 September. Manchester. *Linkman Conference and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

26–29 September. Thessaloniki. *First Congress on Anesthesiology and Intensive Medicine.*
Information: Society of Anesthesiologists and Intensivists of Northern Greece 4, Aristotelous Square, 546 32 Thessaloniki, Greece.

1–3 October. London. *International Meeting jointly sponsored by The Royal Society of Medicine and The New York Academy of Sciences. Advances in the understanding and treatment of asthma.*
Information: Fiona Morris, The Royal Society of Medicine, 1 Wimpole Street, London, W1M 8AE.

8–10 October. Rotterdam. *Eleventh International Symposium on Information Technology in Anesthesia, Intensive Care and Cardiopulmonary Medicine.*
Information: Dr Omar Prakash, Chief, Thorax Anesthesia, Thorax Centre, Erasmus University, 3000 DR Rotterdam, The Netherlands.

13 October. London. *Postgraduate Study day with the College of Anaesthetists.*
Information: College of Anaesthetists, 35 Lincoln's Inn Fields, London, WC2.

19–23 October. Las Vegas. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

31 October–2 November. Mainz. *International Symposium. Echocardiography.*
Information: Professor Dr Raimund Erbel, 11. Medical Clinic,

Johannes Gutenberg-University Mainz, Langenbeckstrasse 1, D-6500 Mainz, West Germany.

3–4 November. New York. *28th Annual Bernard H. Eliasberg Memorial Symposium.*
Information: Anita Guffin, MMS, Mount Sinai Medical Center, One Gustave Levy Place, New York, NY 10029, USA.

5–10 November. Sao Paulo. *36th Brazilian Congress of Anesthesiology.*
Information: Dr R. Mathias, Rua Caiubi 666, Sao Paulo, Brazil 05010.

7–9 November. Israel. *Fourth International Symposium of Anaesthesia and Intensive Care.*
Information: Dr G. Gurman, Division of Anaesthesiology, Soroka Medical Centre, Beer-Sheva 84101, Israel.

8–9 November. Pakistan. *Third International Anaesthesia Conference.*
Information: Dr Jamila Bilal, Associate Professor, Secretary Organising Committee, Khushal Khan Road, F/21 Peshawar U/Town, Pakistan.

18–21 November. Kyoto, Japan. *4th International Symposium on the Pain Clinic.*
Information: 4th WSPC Secretariat, Department of Anesthesiology, Osaka Medical College, c/o Inter Group Corp., Shohaku Bldg., 6–23 Chayamachi Kita-ku, Osaka 530, Japan.

5–9 December. San Juan. *15th Caribbean Symposium in Anaesthesia and Related Fields.*
Information: Miguel Colon-Morales, GPO Box 4547, San Juan, Puerto Rico 00936.

8–12 December. New York. *Forty-fourth Postgraduate Assembly in Anesthesiology.*
Information: Kurt G. Becker, Executive Director, The New York State Society of Anesthesiologists Inc., 41 East 42nd Street, Suite 1605, New York 10017, USA.

27–30 December. Madras: *39th Annual Conference Indian Society of Anaesthetists.*
Information: Dr K. Balakrishnan, Organising Secretary, Department of Anaesthesia (Speciality), Government General Hospital, Madras 600 003, India.

1991

10–13 January. Miami. *28th Annual Post-Graduate Seminar in Anesthesiology.*
Information: Barbara McNulty, Continuing Education Programs, 7480 Fairway Drive, Suite 106, Miami Lakes, Florida 33014, USA.

12–19 January. Barbados. *9th Annual Symposium: clinical update in Anesthesiology.*
Information: Ms H. Phillips, Mount Sinai Medical Center, 1 Gustave L. Levy Place, Box 1010, New York, NY 10029, USA.

15–17 January. Doha-Qatar. *First Gulf Conference on Intensive Care Medicine.*
Information: Dr Jamal S. Al-Shanableh, Consultant Cardiac Anesthiologist, Secretary, P.O. Box 3050, Hamad General Hospital, Doha-Qatar.

18–19 January. London. *Winter Scientific Meeting and Technical Exhibition Queen Elizabeth Conference Centre.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

2–9 February. Colorado. *17th Annual Vail Conference in Anesthesiology.*
Information: Sonja Craythorne, Professional Seminars, P.O. Box 012318, Miami, Florida 33101, USA.

8–12 March. San Antonio. *65th Congress of the International Anesthesia Research Society.*
Information: Emerson A. Moffitt, IARS, 3645 Warrensville Center Road, Cleveland, Ohio 44122, USA.

9–14 March. Pretoria. *The 1991 National Anaesthetic Congress of the South African Society of Anaesthetists.*
Information: Professor J.M. Hugo, Chairman, Department of Anaesthetics, Faculty of Medicine, P.O. Box 667, Pretoria, South Africa.

3–5 April. Oxford. *Junior Anaesthetists' Group of the Association of Anaesthetists of Great Britain and Ireland Linkman Conference and Annual Scientific Meeting.*
Information: Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

15–18 April. Hamamatsu, Japan. *6th International Symposium on Computing in Anesthesia and Intensive Care.*
Information: Dr K. Ikeda, Chairman of the Organising Committee, c/o Department of Anesthesiology, Hamamatsu University School of Medicine, 3600 Handa-cho, Hamamatsu, Shizuoka, 431–31 Japan.

18–21 April. Paris. *European Academy of Anaesthesiology. Refresher Course.*
Information: Professor J.M. Desmonts, Department d'Anesthesie, Hopital Bichat, 46 rue Henri-Huchard, 75018 Paris, France.

23–27 April. Montreal. *Second International Symposium on Pediatric Pain.*
Information: Pain Secretariat, 3450 University Street, Montreal, Quebec, H3A 2A7, Canada.

1–4 May. Montreal. *2nd International Symposium on Pediatric Pain.*
Information: Pain Secretariat, 3450 University Street, Montreal, Quebec H3A 2A7, Canada.

3–5 May. Philadelphia. *AUA Annual Meeting.*
Information: Stephen J. Prevoznik, Department of Anesthesia, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania 19104, USA.

9–12 May. Washington DC. *6th International Dental Congress on Modern Pain Control.*
Information: American Dental Society of Anesthesiology, Inc., 211 E. Chicago Avenue, Suite 948, Chicago, IL 60611, USA.

24–25 May. The Netherlands. *Receptors of the Brain, Lung and Heart: State of the Art.*
Information: Cader Research B.V., P.O. Box 85, 4854 ZH Breda/Bavel, The Netherlands.

27–31 May. Montreal. *McGil University Annual Review Course in Anaesthesia.*
Information: Post Graduate Board, Royal Victoria Hospital, 687 Pine Avenue West, Room H308, Montreal Quebec, H3A 1A1, Canada.

21–25 June. Quebec City. *48th Annual Meeting of Canadian Anaesthetists' Society.*
Information: Ms Ann Andrews, CAS, 187 Gerrard St. E., Toronto, Ontario M5A 2E5, Canada.

11–13 September. Harrogate. *Linkman and Annual Scientific Meeting of Association of Anaesthetists of Great Britain and Ireland.*
Information: Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

26–30 October. San Francisco. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

7–11 December. New York. *Forty-fifth Postgraduate Assembly in Anesthesiology.*
Information: Kurt G. Becker, Executive Director, The New York State Society of Anesthesiologists Inc., 41 East 42nd Street, Suite 1605, New York 10017, USA.

1992

1–8 February. Colorado. *18th Annual Vail Conference in Anaesthesiology.*
Information: Sonja Craythorne, Professional Seminars, P.O. Box 012318, Miami, Florida 33101, USA.

13–17 March. San Francisco. *66th Congress of the International Anesthesia Research Society.*
Information: International Anesthesia Research Society, 3645 Warrenville Center Road, Cleveland, Ohio 44122, USA.

29 March–2 April. Atlanta, Georgia. *The Third International Symposium on the History of Anaesthesia.*
Information: R.K. Calverley, Medical Center, University of California, 225 Dickinson Street, San Diego, California CA 92103, USA.

1–3 April. Bristol. *Junior Anaesthetists' Group Linkman Conference and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

7–12 June. Barcelona. *Anestesia 92.*
Information: Pacifico, S.A.: c/Muntaner, 112 08036-Barcelona, Spain.

10–13 June. Brussels. *European Society of Regional Anaesthesia (UK) Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

12–19 June. The Hague. *10th World Congress of Anaesthesiology.*
Information: Dr Harm Lip, Nilantsweg, 99, 8041 AR Zwolle, Netherlands.

9–11 September. Bournemouth. *Linkman and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

17–21 October. New Orleans. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

12–16 December. New York. *46th Postgraduate Assembly in Anesthesiology.*
Information: Kurt G. Becker, Executive Director, The New York State Society of Anesthesiologists, Inc., 41 East 42nd Street, Suite 1605, New York 10017, USA.

1993

12–16 February. Utah. *38th Annual Postgraduate Course in Anesthesiology — 'Anesthesiology: Today and Tomorrow'.*
Information: Vicky Larson, Department of Anesthesiology, University of Utah School of Medicine, 50 North Medical Drive, Salt Lake City, Utah 84132, USA.

29 April–2 March. North Carolina. *Meeting of the Association of University Anesthetists.*
Information: Francis M. James III, Department of Anesthesia, Wake Forest University Medical Center, 300 S. Hawthorne Road, Winston-Salem, North Carolina 27103, USA.

15–17 September. Glasgow. *Joint Meeting between the Association of Anaesthetists of Great Britain and Ireland and the Canadian Anaesthetists' Society.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

22–24 September. Glasgow. *Linkman Conference and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

9–13 October. Washington DC. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA 515 Busse Highway, Park Ridge, IL 60068, USA.

1994

7–9 September. Brighton. *Linkman Conference and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

2–7 October. Jerusalem. *European Congress.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

Safety Action Bulletin

Syringe drivers Dascon IP 300 syringe driver

Over- or under-infusion has occurred with this syringe driver and SAB (90) 29 recommends removal from use as soon as possible. These pumps are now quite old and have no safety alarms.

IVAC 7 11 syringe pumps

A modification is available to reduce the risk of fluid retention within the instrument which may cause these pumps to fail to operate. The Department of Health recommends that this modification be carried out.

Hydrocath triple lumen central venous catheter

Viggo-Spectramed are withdrawing batch 89 OCT 036 AO Hydrocath. The catheter hubs may crack when they are exposed to alcohol-based substances.

Conductive adhesive diathermy neutral return plates: avoidance of patient burns

SAB (90) 37 should be read by everyone who uses self-adhesive diathermy neutral return plates. It is not possible completely to summarise this announcement which is made because there appears to be an increased incidence of burns to patients. There needs to be perfect contact between the plate and the patient; this may include shaving the skin, the avoidance of underlying bony areas, the avoidance of use of plates with dried-out adherent, the avoidance of re-use of single use items and the avoidance of any other conductive pathway between the patient and other metallic equipment.

Erratum

Anaesthesia, 1990, Volume 45, page 185

We are reprinting the Safety Action Bulletin that appeared in the February issue because of a discrepancy between the heading and the rest of the text. It should read:

Safety Action Bulletin

Anaesthetic and respiratory equipment: the use of 22-mm breathing system connexions (SAB) 89 (78)

This announces an internationally agreed change designed to improve the security of 22-mm connexions and reduce their number. It embodies the need to abandon the defined male/female sequence of fittings. Implementation may result in some incompatibilities.

Health Authorities are advised to organise a planned change to the new system to avoid the hazard of disconnexion and misconnexion. The British Anaesthetic and Respiratory Equipment Manufacturers' Association (BAREMA) are prepared to advise about the availability and suitability of equipment supplied by its members. Enquiries should be directed to the Secretary, Mr B. R. Sugg, The Stables, Sugworth Road, Randley, Oxford, OX14 2HX (Tel. 0865 736393).

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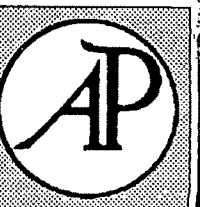

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